BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

# Impact of a modified version of Baby-Led Weaning on iron intake and status: a randomised controlled trial



| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2017-019036 |
| Article Type: | Research |
| Date Submitted by the Author: | 07-Aug-2017 |
| Complete List of Authors: | Daniels, Lisa; University of Otago, Human Nutrition; University of Otago, Medicine<br>Taylor, Rachael; University of Otago, Medicine<br>Williams, Sheila; University of Otago, Preventive and Social Medicine<br>Gibson, R; University of Otago, Human Nutrition<br>Fleming, Elizabeth; University of Otago, Human Nutrition; University of Otago, Medicine<br>Wheeler, Benjamin; University of Otago, Women's and Children's Health<br>Taylor, Barry; University of Otago, Women's and Children's Health<br>Haszard, Jillian; University of Otago, Human Nutrition<br>Heath, Anne-Louise; University of Otago, Human Nutrition |
| Keywords: | Baby-led weaning, Complementary feeding, Dietary iron, Iron status, Iron deficiency, Infants |
| | |



SCHOLARONE™
Manuscripts

For peer review only

# Impact of a modified version of Baby-Led Weaning on iron intake and status: a randomised controlled trial

Lisa Daniels, MDiet[1,2]

Rachael W Taylor, PhD[2]

Sheila M Williams, DSc[3]

Rosalind S Gibson, PhD[1]

Elizabeth A Fleming, MCapSci[1,2]

Benjamin J Wheeler, FRACP[4]

Barry J Taylor, FRACP[4]

Jillian J Haszard, PhD[1]

*Anne-Louise M Heath, PhD[1]

[1]Department of Human Nutrition, University of Otago, PO Box 56, Dunedin 9054, New Zealand

[2]Department of Medicine, University of Otago, PO Box 56, Dunedin 9054, New Zealand

[3]Department of Preventive and Social Medicine, University of Otago, PO Box 56, Dunedin 9054, New Zealand

[4]Department of Women's and Children's Health, University of Otago, PO Box 56, Dunedin 9054, New Zealand

*** Corresponding author**

Anne-Louise M Heath

Department of Human Nutrition

For peer review only

University of Otago

PO Box 56

Dunedin 9054

New Zealand

Telephone: +64 3 479 8379

Email: anne-louise.heath@otago.ac.nz

**Funding statement:** This work was supported by Meat & Livestock Australia, Lottery Health Research, Karitane Products Society, Perpetual Trustees, the University of Otago, and the New Zealand Federation of Women's Institutes. The funders provided funds only and played no role in carrying out the study or the analysis or interpretation of results. Heinz Wattie's Limited provided baby rice cereal for participants in the intervention group. Part of Professor R Taylor's salary is from a Karitane Products Society (KPS) Fellowship that is paid via the University of Otago. Lisa Daniels was supported by a University of Otago Doctoral Scholarship, and a University of Otago Postgraduate Publishing Bursary.

**Competing interests statement:** We have read and understood the BMJ policy on declaration of interests and declare that we have no competing interests.

**Clinical Trial Registration:** Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au). Identifier ACTRN12612001133820.

**Data Sharing Statement:** No additional data are available.

**Abbreviations**

AGP $\alpha_1$-acid glycoprotein

For peer review only

| | |
|---|---|
| BLW | Baby-Led Weaning |
| BLISS | Baby-Led Introduction to SolidS |
| CRP | C-reactive protein |
| EFSA | European Food Safety Authority |
| GP | general practitioner |
| MFP | 'meat, fish, poultry' |
| sTfR | soluble transferrin receptor |
| WDR | weighed three-day diet record |

**Abstract word count:** 268

**Word count:** 3,891

For peer review only

**Abstract**

**Objective:** To determine the iron intake and status of infants following a version of Baby-Led Weaning (BLW) modified to prevent iron deficiency (Baby-Led Introduction to SolidS; BLISS) compared to those of infants following traditional spoon-feeding.

**Design, participants and intervention:** This randomised controlled trial included 206 participants assigned to Control (n=101) or BLISS (n=105) groups. Both groups received standard midwifery and 'Well Child' care. BLISS participants received eight additional visits (from before birth to 9 months) providing education and support on the BLISS approach to complementary feeding (i.e. BLW modified to increase iron intake).

**Outcome measures:** Intake of iron and key absorption modifiers was assessed using weighed three-day diet records at 7 and 12 months. A venipuncture blood sample was collected at 12 months to determine plasma ferritin, haemoglobin, soluble transferrin receptor, C-reactive protein, and $\alpha_1$-acid glycoprotein concentrations; and body iron was calculated.

**Results:** Differences in median dietary iron intakes between the Control and BLISS groups were not significant at 7 (difference 0.6 mg/day; 95% CI: -1.0 to 2.3) or 12 (-0.1 mg/day; -1.6 to 1.4) months of age. Similarly, there were no significant differences in plasma ferritin concentration (difference -2.6 μg/L; 95% CI: -10.9 to 5.8), body iron (0.04 mg/kg; -1.1 to 1.2), or the prevalence of depleted iron stores, early functional iron deficiency, or iron deficiency anaemia (all $p \geq 0.65$) at 12 months of age.

**Conclusions:** A baby-led approach to complementary feeding does not appear to increase the risk of iron deficiency in infants when their parents are given advice to offer 'high-iron' foods with each meal.

**Trial registration:** Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au). Identifier ACTRN12612001133820.

For peer review only

**Keywords:** Baby-led weaning, complementary feeding, dietary iron, iron status, iron deficiency, body iron, infants, toddlers

For peer review only

## Article summary

### Strengths and limitations of this study:

- First randomised controlled trial to investigate the impact of a baby-led approach to complementary feeding on iron intake and biochemical iron status.
- Robust dietary assessment data provided by weighed diet records collected on non-consecutive days.
- Did not reach planned sample size, but confidence intervals are provided to indicate the range of plausible values in the population.
- This trial cannot be used to draw conclusions about the risk of iron deficiency in infants following unmodified BLW.

For peer review only

## Introduction

Anecdotal reports suggest that many parents are following Baby-Led Weaning (BLW) with their infants, particularly in New Zealand,[1] the United Kingdom,[2] and Canada.[3] However, health professionals have expressed concerns about this alternative approach to complementary feeding that need to be addressed.[3,4] Infants following BLW are expected to feed themselves *all* of their food from the start of the complementary feeding period[5] and it has been proposed that this may increase the risk of iron deficiency if the majority of first foods offered are foods low in iron, such as fruits and vegetables, or if iron-fortified infant cereals are avoided due to their semi-liquid consistency.[6] A recent observational study reported that mean dietary iron intake in infants following BLW was less than half that of infants following traditional spoon-feeding.[6] However, the impact of this lower iron intake on the biochemical iron status of infants has not been examined in that[6] or any other study.

Iron deficiency that progresses to iron deficiency anaemia can impact on the central nervous system and development during infancy, leading to poorer cognitive and behavioural performance.[7] Moreover, these impacts on infant development may not be reversible.[8,9] It is important, therefore, to determine whether a baby-led approach can be followed without increasing the risk of iron deficiency before baby-led approaches can be considered an appropriate alternative to traditional complementary feeding practices.

The aim of the Baby-led Introduction to SolidS (BLISS) study was to determine whether a modified version of BLW prevents young children from becoming overweight,[10] without increasing their risk of iron deficiency, growth faltering,[10] and choking.[11] In this paper we report the iron intake (at 7 and 12 months of age) and status (at 12 months) of infants following BLISS compared with traditional spoon-feeding.

For peer review only

## Methods

Detailed methods have been described elsewhere[12] so only relevant information is included here. The Lower South Regional Ethics Committee (LRS/11/09/037) approved the study and adult participants gave written informed consent. Pregnant women in their third trimester of pregnancy who were booked into the Queen Mary Maternity Hospital in Dunedin, New Zealand were invited into the study between November 2012 and March 2014. Women were eligible if they: spoke English or Te Reo Māori (the indigenous language of New Zealand); planned to live in Dunedin, New Zealand, until their child was at least 2 years of age; and were 16 years of age or older. Women were excluded if their infant was born before 37 weeks gestation, or had a congenital abnormality, physical condition or intellectual disability that was likely to affect their feeding or growth. Participants were randomised using random length blocks after stratification for parity (first child, subsequent child) and maternal education (tertiary, non-tertiary), to Control (n=101) or BLISS (n=105) groups by the study biostatistician.

## Intervention

The Control group participants received routine midwifery (until 6 weeks of age) and 'Well Child' care (from 6 weeks). 'Well Child Tamariki Ora' is a nationally funded program to support and educate families with children under 5 years of age.[13]

Participants in the BLISS group received routine midwifery and 'Well Child' care, and BLISS support and education from before birth (approximately 34-35 weeks gestation) until 9 months of age. The BLISS approach was based on three key principles of BLW: exclusive milk feeding until 6 months of age, infant self-feeding from the start of complementary feeding (i.e. baby-led), and offering family foods as finger foods so they can be picked up by

For peer review only

the infant. However, BLISS also included modifications to address the three main concerns about BLW expressed by health professionals:[3,4] iron deficiency, growth faltering,[10] and choking.[11]

The BLISS intervention comprised: 1) five contacts with a lactation consultant (from the third trimester of pregnancy to 6 months of age) to encourage and support exclusive milk feeding (ideally breastfeeding) and delay the introduction of complementary foods until 6 months of age, 2) three contacts with BLISS research staff to give individualised advice on how to follow BLISS (at 5.5, 7 and 9 months of age), and 3) a range of written resources that were developed to help parents follow BLISS,[14] including recipe books given at 5.5, 7 and 9 months of age, and lists of age-appropriate foods.[12] Parents were encouraged to offer their child three types of finger foods at every meal: a 'high-iron' food (e.g., red meat, iron-fortified infant cereal (in a hand held way, e.g., on toast)), an energy rich food (>1.5 kcal/g, e.g., avocado, cheese), and an easy to eat food such as fruit or vegetables. BLISS participants were provided with complementary packets of iron-fortified infant cereal (For Baby Rice Cereal, Heinz Watties Ltd., Australia) at each of the intervention visits (5.5, 7, and 9 months). The iron content of this infant cereal was 2.2 mg per 100 g of infant cereal prepared with water.

**Adherence**

Questionnaires were used to determine adherence to BLISS by asking parents 'how has your baby been fed solids in the past week?' when their infant was 7 and 12 months of age. Adherence to BLISS was defined as the infant feeding themselves most or all of their food in the past week.

For peer review only

**Outcome Assessment**

Demographic data were collected at baseline by questionnaire, except for birth weight and gestational age which were obtained from hospital records. Research staff conducting measurement visits and administering questionnaires were blinded to group allocation. At 2, 4, 6, 7, 8, 9 and 12 months of age brief feeding questionnaires were used to collect information including the age when breastfeeding stopped and/or formula feeding started and stopped.

***Dietary Assessment***

Weighed three-day diet records (WDRs) were used to assess dietary intake at 7 and 12 months of age. Parent participants were given detailed instructions and provided with dietary scales (Salter Electronic, Salter Housewares Ltd. Tonbridge, UK) accurate to ±1 g. They then recorded everything their child ate and drank over three randomly assigned non-consecutive days (two week days and one weekend day) over a three week period. Parents were asked to record the total weight of food offered, and to collect, weigh and record all leftover food including food on the floor, baby, or the tray, so that the amount of food consumed by the infant could be calculated. Any supplements consumed were also recorded.

The WDRs were entered into Kai-culator (Version 1.13s, University of Otago, New Zealand), a dietary analysis program that includes dietary data from the New Zealand Food Composition Database (FOODfiles 2010, Plant and Food Research),[15] commonly consumed recipes from the 2008/09 New Zealand Adult Nutrition Survey,[16] and commercial infant foods collated by the research team.[17] It was not possible to directly measure breast milk intake so it was assumed to be 750 g per day at 7 months and 448 g per day at 12 months based on a quadratic curve fitted to the breast milk volumes reported by Dewey et al.[18] The iron content of breast milk was assumed to be 0.07 mg per 100 g.[15] If

For peer review only

the infant was fed both breast milk and infant formula then the gram amount of infant formula consumed was subtracted from the estimated total breast milk intake (i.e. 750 or 448 g per day).

Grams of red meat, grams of 'meat, fish, poultry' (MFP), milligrams of haem iron,[19] and milligrams of phytate[20] were determined using values from the literature and information from manufacturers.

***Biochemical Assessment***

A non-fasting venous blood sample was obtained from 119 of the 145 infants whose parents consented to the blood test at 12 months of age (82%, which was 58% of total study participants). Of those who did not consent, 22 had withdrawn from the study by 12 months of age, 13 could not be contacted or were living out of town, and 26 refused the blood test. Blood samples were drawn from an antecubital vein into a trace element-free lithium heparin anticoagulated tube (7.5 mL; S-Monovette, Sarstedt, Nümbrecht, Germany) and refrigerated immediately after collection. If the child was unwell the blood test was delayed for 14 days.

Complete blood count (Sysmex XE 5000, Kobe, Japan) and plasma ferritin (Cobas 8000 unit e 602, Roche, USA) were determined on collection day by Southern Community Laboratories Ltd., (Dunedin, New Zealand). Aliquots of plasma were stored at ⁻80°C until subsequent analysis of soluble transferrin receptor (sTfR), C-reactive protein (CRP), and $\alpha_1$-acid glycoprotein (AGP), using a Cobas C311 (Roche, USA) at the Department of Human Nutrition laboratories (University of Otago, Dunedin, New Zealand). Cutoffs of > 5 mg/L CRP and > 1 g/L AGP defined the presence of inflammation, for example as a result of infection. Ferritin multipliers were used to adjust ferritin concentrations to remove the

For peer review only

influence of this inflammation.[21] The sTfR values were converted to be equivalent with the Flowers assay:[22] 1.5 x Roche sTfR + 0.35 mg/L and body iron (mg/kg) was calculated:[22] -[log10(sTfR x 1000/ferritin) -2.8229]/0.1207.

**Adverse Events**

Participants with biochemical results outside pre-defined clinical reference ranges for Complete Blood Count indices or plasma ferritin were contacted, informed of the abnormal result, and advised to visit their general practitioner for advice.

**Statistical Analysis**

The data were analysed according to modified intention to treat. A sample size of 84 participants per group provided 80% power ($\alpha$=0.05) to detect a difference in geometric mean plasma ferritin concentrations of 5.0 µg/L.[12]

The proportions of infants at 7 and 12 months of age fed breast milk, infant formula, or both ('mixed fed'), as well as those consuming cow's milk were determined using Chi-squared tests. All nutrient and food group data are presented as daily averages over the three days. As most variables were positively skewed, the data are reported as medians and lower and upper quartiles ($25^{th}$ and $75^{th}$). Quantile regression was used to estimate the difference between the Control and BLISS groups for energy and nutrient intake, as well as dietary iron intake from each food group. Usual iron intake was determined,[23] and the prevalence of inadequate iron intakes was estimated using the full-probability approach.[24]

Means and standard deviations are used to describe all of the biochemical variables except plasma ferritin, CRP and AGP, which are presented as medians and lower and upper quartiles.

For peer review only

Differences in biochemical iron status indices were estimated using regression and were adjusted for infant age at the time of blood test, infant sex, maternal education (non tertiary vs tertiary) and maternal parity (1 child vs > 1 child, including the current pregnancy). A Chi-squared test was used to compare the number of cases and controls for each of the iron status categories, and their associated odds ratios.

All analyses were conducted using statistical software Stata, version 13 (StataCorp LP, Texas, USA).

**Results**

A total of 214 mother-infant pairs were randomised, of whom eight were excluded after birth (n=5 Control, n=3 BLISS), providing a final sample size of 206 participants (**Figure 1**). Baseline demographic data, and age when complementary foods were introduced, are shown in **Table 1**. Adherence to the baby-led approach was high in the BLISS group with significantly more infants feeding themselves most or all of their food in the past week at 7 (74% vs 19% Control; $p<0.001$) and 12 (77% vs 48% Control; $p<0.001$) months of age. There was no difference in the number of infants who were fed breast milk, formula or both, between groups at either 7 or 12 months (**eTable 1**).

There were no statistically significant differences in dietary iron intakes between the groups at either 7 or 12 months of age (adjusted difference at 7 months 0.6 mg/day; 95% CI: -1.0 to 2.3; **Table 2**), or in intakes of iron absorption modifiers, except for a significantly lower intake of Vitamin C in BLISS (49.2 mg/day) compared with Control infants (59.2 mg/day) at 7 months (adjusted difference -9.7 mg/day; 95% CI: -18.4 to -0.9). Four participants (n=2 BLISS; n=2

For peer review only

Control) were using iron supplements at the time of the 12-month WDR but these have not been included as the supplements were started after the blood sample was collected.

There were no significant differences in estimated breast milk or infant formula intake between groups at 7 (breast milk difference 0.0 g/day; 95% CI: -5.1 to 5.1; $p$=1.00; infant formula difference 216 g/day; -97.2 to 530; $p$=0.17) or 12 (breast milk difference 0.0 g/day; 95% CI: -0.1 to 0.1; $p$=0.94; infant formula difference -85 g/day; -277 to 107; $p$=0.38) months of age, and therefore no differences between groups in the contribution of infant milks to iron intake (all $p$>0.17).

BLISS infants obtained significantly more iron from 'breads and cereals', 'red meat', 'dairy', and 'legumes, nuts, seeds and eggs' than Control infants at 7 months of age (**Table 3**). For all these food groups, except 'breads and cereals', this reflected the greater proportion of BLISS infants consuming these foods (**eTable 2**). However, the differences in iron contribution were small (e.g., adjusted difference 0.1 mg iron/day from red meat; 95% CI: 0.01 to 0.1) in comparison to the Average Requirement of 5.0 mg/day[26] and therefore not likely to be clinically significant. None of the differences apparent at 7 months remained at 12 months, and although BLISS infants did receive significantly less iron from 'vegetables' than Control infants at 12 months, the actual difference was very small (-0.1 mg iron/day; 95% CI: -0.2 to -0.0) (Table 3).

BLISS specifically encouraged consumption of 'high-iron' foods such as red meat and iron-fortified infant cereal from the start of complementary feeding. BLISS infants were introduced to 'red meat' at the same age as Control infants (28.1 weeks, 27.9 weeks, $p$=0.74). Although significantly more BLISS than Control infants consumed 'red meat' at 7 months of

For peer review only

age (76%, 55%; eTable 2), intakes were similarly low for consumers in both groups (BLISS 3.2 g/day, Control 3.8 g/day; **eTable 3**). BLISS infants began consuming 'iron-fortified infant cereal' approximately two weeks later than Control infants (25.4 weeks, 23.7 weeks, $p$=0.008). Interestingly, more BLISS infants were consuming 'iron-fortified infant cereal' by 7 months of age (73%, 51% Control) (eTable 2), but the median amounts consumed were very small (BLISS 1.7 g/day, Control 4.0 g/day) (eTable 3). At 12 months there were no significant differences in the number of consumers of 'iron-fortified infant cereal' or 'red meat', or in the amount consumed (**eTables 4 and 5**).

The prevalence of inadequate iron intakes was high at 74% for both groups at 7 months of age, but considerably lower by 12 months (Control 23%, BLISS 26%).

There were no statistically significant differences between the groups in any of the biochemical indicators of iron status (all $p$>0.55) (**Table 4**). Few participants had signs of inflammation/infection (n=8 Control, n=11 BLISS). The majority of infants in both groups were iron sufficient (83% Control, 83% BLISS), although 5% Control and 7% BLISS presented with iron deficiency anaemia (Table 4). Similar numbers had anaemia other than iron deficiency anaemia (13% BLISS, 10% Control; $p$=0.78).

Thirty-four participants had at least one biochemical value (not necessarily iron-related) outside the expected reference range for their age and were advised to contact their GP for follow up (Control: n=19, BLISS: n=15).

**Discussion**

For peer review only

We observed no significant differences in iron intake or status between infants following a baby-led approach to complementary feeding that had been modified to address concerns regarding iron intake, and infants following traditional spoon-feeding. However, iron intakes were low in both groups at 7 months (74% of infants at risk of inadequate intakes) and 17% had suboptimal iron status at 12 months.

Although many parents are choosing to follow BLW with their infant,[1-3] we know almost nothing about what these infants are eating, and how this might impact their health. Only one small observational study has evaluated intake in infants following unmodified BLW compared with age- and sex-matched infants following traditional spoon-feeding.[6] In that study, despite similar energy intakes, BLW infants had significantly lower intakes of iron than spoon-fed infants (1.6 mg/day vs 3.6 mg/day, $p<0.001$). By contrast, we found no difference in iron intakes in our study groups, and BLISS infants were consuming a median of 3.0 mg per day of iron, suggesting that encouraging the intake of 'high-iron' foods as part of a baby-led approach to complementary foods was effective in improving iron intakes.

Our BLISS intervention recommended that 'high-iron' foods, particularly red meat and iron-fortified infant cereal, should be offered at every meal, from the start of the complementary feeding period. Red meat is high in bioavailable haem iron,[27] and a higher intake has been associated with higher serum ferritin concentrations in toddlers,[28] and higher haemoglobin concentrations in very young children.[29] Similarly, iron-fortified infant cereal is high in iron and consumption has been shown to prevent iron deficiency anaemia.[30] In the current study, significantly more BLISS than Control infants were consuming red meat at 7 months. This was in contrast to an observational study suggesting that infants following unmodified BLW are no more likely to consume red meat than spoon-fed infants.[6] However, actual

For peer review only

intakes were small in both groups, as they were for iron-fortified infant cereal. Other studies have also demonstrated relatively low intakes of both red meat[31] and iron fortified foods[32] in infants and toddlers. Therefore, further research is required to determine whether a more intensive intervention can feasibly increase the amount of these important iron sources consumed by both spoon-fed and baby-led infants.

Concern has been expressed regarding dietary exposure to inorganic arsenic through infant rice cereals and the potential health risks associated with high intakes in very young children.[33] Intakes of 3.0 μg/kg body weight per day have been estimated to increase the incidence of lung cancer by 0.5%,[34] and the European Food Safety Authority (EFSA) have estimated that a 6 month old infant would have to consume 90 g of rice based cereal per day in order to be exposed to a level of inorganic arsenic of approximately half that level (1.63 μg/kg body weight).[33] Given the maximum average intake in the current study was only 7.2 g per day of infant rice cereal, and the maximum observed intake was 75 g per day, it seems very unlikely that high intakes of inorganic arsenic are an issue in this population, even when consumption of iron fortified rice cereal is encouraged.

The current study suggests that when parents following a baby-led approach to complementary feeding are given advice to offer infants 'high-iron' foods with every meal, their iron status is similar to Control infants. This finding is important given health professionals' concerns that baby-led approaches to complementary feeding may increase the risk of iron deficiency,[3,4] and the observation that infants following unmodified BLW have significantly lower iron intakes.[6] Although we did not reach our planned sample size, it is important to note the most extreme difference in plasma ferritin concentration consistent with the data was -10.9 μg/L (i.e. the lower confidence limit for the difference). This suggests that,

For peer review only

in response to a BLISS intervention, the Control group's median plasma ferritin concentration might, at most, fall to 18.0 μg/L – a value above the cutoffs usually associated with deficiency (i.e. 12 or 15 μg/L). The data are also consistent with plasma ferritin rising to 34.7 μg/L (applying the upper confidence limit).

Our study has a number of strengths including being the first randomised controlled trial to investigate the impact of a baby-led approach to complementary feeding on iron intake and status. We collected robust dietary data using three non-consecutive days of weighed diet records. As infants often do not eat all of the food offered to them we asked parents to weigh the food before and after eating (including food that was no longer on the surface on which it was originally offered) to ensure we had as accurate a representation of actual consumption as was possible in a free-living population. The study had limited power to detect differences of 5.0 μg/L in geometric mean plasma ferritin concentrations because blood samples were obtained from 119 participants rather than the planned 168. However, the confidence intervals enable the reader to see the range of plausible differences in plasma ferritin between the groups. Finally, it was not considered ethical to randomise participants to follow an unmodified version of BLW because of concerns about its safety.[3,4] Therefore, the results should not be used to make conclusions about the iron status of infants following unmodified BLW.

**Conclusions**

There was no evidence of a difference in iron intakes and status between spoon-fed infants and infants following this modified version of BLW in which parents were given advice to offer 'high-iron' foods with each meal. This suggests that a baby-led approach can be used without impacting negatively on iron status. However, it is important to note that this study

For peer review only

assessed a modified version of BLW so no conclusions can be made about the risk of iron deficiency in infants following unmodified BLW.

**Acknowledgments**

We would like to acknowledge all the families who participated in the BLISS study, as well as the research staff involved from the Departments of Human Nutrition and Medicine at the University of Otago.

For peer review only

**Figure legend**

**Figure 1.** Flow of participants through the study

**Table legend**

**Table 1.** Characteristics of participants who provided intake data at 7 (n=162) and/or 12 (n=143) months of age or biochemical data at 12 (n=119) months of age

**Table 2.** Intake of iron and key absorption modifiers at 7 and 12 months of age from complementary foods and infant milks[a]

**Table 3.** Iron from complementary foods at 7 and 12 months of age (consumers and non-consumers)[a,b]

**Table 4.** Iron status indicators and categories at 12 months of age

For peer review only

## References

1 Cameron SL, Taylor RW, Heath A-LM. Parent-led or baby-led? Associations between complementary feeding practices and health-related behaviours in a survey of New Zealand families. *BMJ Open* 2013;**3**:1–9.

2 Brown, Lee. A descriptive study investigating the use and nature of baby-led weaning in a UK sample of mothers. *Maternal Child Nutr* 2011;**7**:34–47.

3 D'Andrea E, Jenkins K, Mathews M. Baby-led Weaning: A Preliminary Investigation. *Can J Diet Pract Res* 2016;**77**:1–6.

4 Cameron SL, Heath A-LM, Taylor RW. Healthcare professionals' and mothers' knowledge of, attitudes to and experiences with, Baby-Led Weaning: a content analysis study. *BMJ Open* 2012;**2**:1–9.

5 Rapley G, Murkett T. *Baby-led Weaning: Helping your Baby to Love Good Food*. London: Vermillon 2008.

6 Morison BJ, Taylor RW, Haszard JJ, *et al.* How different are baby-led weaning and conventional complementary feeding? A cross-sectional study of infants aged 6–8 months. *BMJ Open* 2016;**6**:1–11.

7 Domellöf M, Braegger C, Campoy C, *et al.* Iron requirements of infants and toddlers. *J Pediatr Gastroenterol Nutr* 2014;**58**:119–29.

8 Lozoff B, Beard J, Connor J, *et al.* Long-Lasting Neural and Behavioral Effects of Iron Deficiency in Infancy. *Nut Rev* 2006;**64**:34–43.

9 Congdon EL, Westerlund A, Algarin CR, *et al.* Iron Deficiency in Infancy is Associated with Altered Neural Correlates of Recognition Memory at 10 Years. *J Pediatr* 2012;**160**:1027–33.

10 Taylor RW, Williams SM, Fangupo LJ, *et al.* Effect of a Baby-Led Approach to Complementary Feeding on Infant Growth and Overweight. *JAMA Pediatr* Published online July 10 2017.

11 Fangupo LJ, Heath A-LM, Williams SM, *et al.* A Baby-Led Approach to Eating Solids and Risk of Choking. *Pediatrics* 2016;**138**:1–10.

12 Daniels L, Heath A-LM, Williams SM, *et al.* Baby-Led Introduction to SolidS (BLISS) study: a randomised controlled trial of a baby-led approach to complementary feeding. *BMC Pediatr* 2015;**15**:1–15.

13 Ministry of Health NZ. Well Child/Tamariki Ora services. Wellington: 2014. http://www.health.govt.nz/our-work/life-stages/child-health/well-child-tamariki-ora-services.

14 Cameron SL, Taylor RW, Heath AM. Development and pilot testing of Baby-Led Introduction to SolidS - a version of Baby-Led Weaning modified to address concerns about iron deficiency, growth faltering and choking. *BMC Pediatr* 2015;**15**:1–11.

For peer review only

15 Ministry of Health. New Zealand food composition database (FOODfiles). 2010. www.foodcomposition.co.nz/foodfiles.

16 Ministry of Health, University of Otago. Methodology report for the 2008/09 New Zealand adult nutrition survey. Wellington: 2011. http://www.health.govt.nz/publication/methodology-report-2008-09-nz-adult-nutrition-survey9-new-zealand-adult-nutrition-survey/oclc/756914555.

17 Clousten A. *The role of commercial processed baby foods in the diets of New Zealand toddlers*. Thesis, Master of Dietetics. University of Otago. 2014. http://hdl.handle.net/10523/5492.

18 Dewey KG, Heinig MJ, Nommsen LA, *et al.* Adequacy of energy intake among breast-fed infants in the DARLING study: relationships to growth velocity, morbidity, and activity levels. *J Pediatr* 1991;**119**:538–47.

19 Barris A. *Meat and haem iron intakes of New Zealand toddlers aged 12-24 months*. Thesis, Master of Dietetics. University of Otago. 2012. http://hdl.handle.net/10523/3839.

20 Hartley N. *Phytate and zinc intakes of toddlers from New Zealand*. Thesis, Master of Dietetics. University of Otago. 2013. http://hdl.handle.net/10523/4645.

21 Thurnham DI, McCabe LD, Haldar S, *et al.* Adjusting plasma ferritin concentrations to remove the effects of subclinical inflammation in the assessment of iron deficiency: a meta-analysis. *Am J Clin Nutr* 2010;**92**:546–55.

22 Cogswell ME, Looker AC, Pfeiffer CM, *et al.* Assessment of iron deficiency in US preschool children and nonpregnant females of childbearing age: National health and nutrition examination survey 2003-2006. *Am J Clin Nutr* 2009;**89**:1334–42.

23 Harttig U, Haubrock J, Knüppel S, *et al.* The MSM program: web-based statistics package for estimating usual dietary intake using the Multiple Source Method. *Eur J Clin Nutr* 2011;**65**:S87–S91.

24 Gibson RS, Ferguson EL. An interactive 24-hour recall for assessing the adequacy of iron and zinc intakes in developing countries. *HarvestPlus Technical Monograph* 2008:1–160.

25 Atkinson J, Salmond C, Crampton P. *NZDep2013 Index of Deprivation User's Manual*. Department of Public Health, University of Otago, Wellington and Division of Health Sciences 2014.

26 European Food Safety Authority (EFSA) Panel on Dietetic Products Nutrition and Allergies. Scientific Opinion on Dietary Reference Values for Iron. 2015:1–115.

27 Lombardi-Boccia G, Dominguez BM, Aguzzi A. Total heme and non-heme iron in raw and cooked meats. *Food Chem Toxicol* 2002;**67**:1–4.

28 Szymlek-Gay EA, Ferguson EL, Heath A-LM, *et al.* Food-based strategies

For peer review only

improve iron status in toddlers: a randomized controlled trial. *Am J Clin Nutr* 2009;**90**:1541–51.

29 Olaya GA, Lawson M, Fewtrell MS. Efficacy and safety of new complementary feeding guidelines with an emphasis on red meat consumption: a randomized trial in Bogota, Colombia. *Am J Clin Nutr* 2013;**98**:983–93.

30 Walter T, Dallman PR, Pizarro F, *et al.* Effectiveness of iron-fortified infant cereal in prevention of iron-deficiency anemia. *Pediatrics* 1993;**91**:976–82.

31 Fox MK, Reidy K, Novak T, *et al.* Sources of Energy and Nutrients in the Diets of Infants and Toddlers. *J Am Diet Assoc* 2006;**106**:S28–S42.

32 Wall CR, Brunt DR, Grant CC. Ethnic variance in iron status: is it related to dietary intake? *PHN* 2008;**12**:1413–21.

33 European Food Safety Authority (EFSA) Panel on Contaminants in the Food Chain (CONTAM). Scientific Opinion on Arsenic in Food. *EFSA Journal* 2009;**7**:1351–199.

34 World Health Organization. Joint FAO/WHO Expert Committee On Food Additives: Summary and Conclusions. 2010:1–16.

For peer review only

**Author contributions:**

Mrs Daniels contributed to the design of the iron-related components of the research project, collected data, and prepared the first full and subsequent drafts of this manuscript.

Professor R Taylor is a co-Principal Investigator of the BLISS study, co-designed the research project, made an important intellectual contribution to this manuscript, and approved the final manuscript as submitted.

Associate Professor Heath is a co-Principal Investigator of the BLISS study, co-designed the research project, made an important intellectual contribution to this manuscript, and approved the final manuscript as submitted.

Professor Williams advised on study design and performed statistical analyses, made an important intellectual contribution to this manuscript, and approved the final manuscript as submitted.

Dr Haszard performed statistical analyses, made an important intellectual contribution to this manuscript, and approved the final manuscript as submitted.

Professor Gibson provided expert input into the design of the study and ongoing advice and support, made an important intellectual contribution to this manuscript, and approved the final manuscript as submitted.

For peer review only

Mrs Fleming provided expert input into the design of the study and ongoing advice and support, made an important intellectual contribution to this manuscript, and approved the final manuscript as submitted.

Dr Wheeler provided expert input into the design of the study and ongoing advice and support, made an important intellectual contribution to this manuscript, and approved the final manuscript as submitted.

Dr B Taylor provided expert input into the design of the study and ongoing advice and support, made an important intellectual contribution to this manuscript, and approved the final manuscript as submitted.

For peer review only

**Table 1** Characteristics of participants who provided intake data at 7 (n=162) and/or 12 (n=143) months of age or biochemical data at 12 (n=119) months of age

| | Control (n=81) | BLISS (n=88) |
|---|---|---|
| **Maternal and household variables** | | |
| Maternal age at birth (years), mean (SD) | 32.2 (5.8) | 31.7 (4.8) |
| Maternal parity | | |
| First child | 32 (40) | 37 (42) |
| Two children | 27 (33) | 37 (42) |
| Three or more children | 22 (27) | 14 (16) |
| Maternal ethnicity | | |
| NZ European | 70 (87) | 71 (80) |
| Māori | 6 (7) | 8 (9) |
| Other | 5 (6) | 9 (10) |
| Maternal education | | |
| School only | 23 (28) | 26 (30) |
| Post-secondary | 13 (16) | 20 (22) |
| University | 45 (56) | 42 (48) |
| Household deprivation[a] | | |
| 1-3 (Low) | 24 (30) | 25 (28) |
| 4-6 | 37 (45) | 46 (53) |
| 7-10 (High) | 20 (25) | 17 (19) |
| **Infant variables** | | |
| Sex | | |

For peer review only

| | | |
|---|---|---|
| Female | 37 (46) | 50 (57) |
| Male | 44 (54) | 38 (43) |
| Infant birth weight (g), mean (SD) | 3510 (453) | 3496 (448) |
| Infant gestational age at birth (weeks), mean (SD) | 39.5 (1.2) | 39.7 (1.0) |
| **Complementary feeding variables** | | |
| Age complementary foods were introduced (weeks), mean (SD) | 22.6 (3.1) | 24.6 (3.2)[b] |
| Complementary foods delayed to 6 months of age | 15 (18) | 58 (66)[b] |

Abbreviation: NZ European; New Zealand European
Data presented as n (%), unless otherwise stated
[a]Household deprivation categorised using the NZDep2013 scale in which decile 1 indicates the lowest level of deprivation and 10 indicates the highest[25]
[b]$p<0.001$

For peer review only

**Table 2** Intake of iron and key absorption modifiers at 7 and 12 months of age from complementary foods and infant milks[a]

| | Control | BLISS | Difference (95% CI)[b] | *p* Value |
|---|---|---|---|---|
| **7 months of age** | n=77 | n=85 | | |
| Energy (kJ/day), mean (SD) | 2862 (548) | 2996 (613) | 145 (-31.2, 321) | 0.11 |
| Energy from complementary foods only (kJ/day)[c], mean (SD) | 672 (506) | 799 (595) | 144 (-26.2, 314) | 0.10 |
| Dietary iron (mg/day) | 2.7 (1.3, 6.9) | 3.0 (1.5, 7.3) | 0.6 (-1.0, 2.3) | 0.46 |
| Dietary iron from complementary foods only (mg/day)[d] | 1.0 (0.5, 2.2) | 1.2 (0.7, 2.0) | 0.2 (-0.2, 0.6) | 0.34 |
| Haem iron (mg/day) | 0.0 (0.0, 0.1) | 0.0 (0.0, 0.1) | 0.0 (-0.0, 0.1) | 0.10 |
| Non-haem iron (mg/day) | 2.6 (1.3, 6.9) | 2.9 (1.4, 7.3) | 0.4 (-1.3, 2.0) | 0.67 |
| Meat, fish, poultry (g/day) | 2.8 (0.0, 11.1) | 4.3 (1.4, 8.8) | 1.3 (-1.9, 4.4) | 0.42 |
| Phytate (mg/day) | 36 (16.3, 75.2) | 45 (23.0, 77.6) | 4.2 (-15.0, 23.4) | 0.67 |
| Phytate:iron molar ratio[e] | 1.0 (0.4, 2.3) | 1.3 (0.6, 2.7) | 0.4 (-0.2, 1.0) | 0.18 |
| Vitamin C (mg/day) | 59.2 (41.7, 75.6) | 49.2 (38.3, 67.9) | -9.7 (-18.4, -0.9) | **0.032** |
| **12 months of age** | n=68 | n=75 | | |
| Energy (kJ/day), mean (SD) | 3573 (776) | 3623 (1048) | 109 (-191, 409) | 0.48 |
| Energy from complementary foods only (kJ/day)[c], mean (SD) | 2400 (848) | 2527 (1183) | 195 (-142, 533) | 0.25 |
| Dietary iron (mg/day) | 5.3 (3.1, 8.4) | 4.7 (3.1, 7.3) | -0.1 (-1.6, 1.4) | 0.87 |
| Dietary iron from complementary foods only (mg/day)[d] | 3.2 (2.3, 4.6) | 3.2 (2.5, 4.1) | -0.0 (-0.6, 0.6) | 0.94 |
| Haem iron (mg/day) | 0.2 (0.1, 0.3) | 0.2 (0.1, 0.3) | 0.0 (-0.0, 0.1) | 0.57 |
| Non-haem iron (mg/day) | 5.0 (2.9, 8.1) | 4.5 (2.9, 7.0) | -0.1 (-1.7, 1.4) | 0.85 |

For peer review only

| | | | | |
|---|---|---|---|---|
| Meat, fish, poultry (g/day) | 19.3 (7.9, 33.6) | 19.3 (11.2, 31.1) | -1.4 (-9.0, 6.2) | 0.72 |
| Phytate (mg/day) | 187 (118, 310) | 229 (152, 274) | 37 (-20.4, 94.8) | 0.20 |
| Phytate:iron molar ratio[e] | 3.8 (2.3, 6.2) | 4.3 (2.8, 6.5) | 0.6 (-0.7, 1.9) | 0.35 |
| Vitamin C (mg/day) | 48.1 (39.4, 69.5) | 50.4 (36.6, 61.4) | 0.4 (-9.4, 10.3) | 0.93 |

Data presented as median ($25^{th}$, $75^{th}$ percentile), unless otherwise stated

[a]Intake reported during the three-day weighed diet records collected at 7 and 12 months of age

[b]Difference adjusted for infant age and sex, and maternal education and parity

[c]Excludes energy from breast milk and infant formula

[d]Excludes iron from breast milk and infant formula

[e]Calculated as [phytate (mg) / 660] / [iron (mg) / 55.9]

For peer review only

**Table 3** Iron from complementary foods at 7 and 12 months of age (consumers and non-consumers)[a,b]

| | Control | | BLISS | | Difference (95% CI)[d] | *p* Value |
|---|---|---|---|---|---|---|
| | mg/day | %[c] | mg/day | %[c] | | |
| **7 months of age** | n=77 | | n=85 | | | |
| Vegetables | 0.16 (0.0, 0.4) | 17 (9, 25) | 0.10 (0.0, 0.2) | 8.4 (6, 17) | -0.1 (-0.1, 0.0) | 0.07 |
| Fruit and fruit juice | 0.13 (0.0, 0.2) | 11 (5, 24) | 0.09 (0.0, 0.2) | 7.2 (3, 12) | -0.0 (-0.1, 0.0) | 0.19 |
| Iron-fortified infant cereal | 0.08 (0.0, 0.7) | 7.9 (0, 54) | 0.19 (0.0, 0.5) | 19 (0, 43) | 0.1 (-0.1, 0.3) | 0.25 |
| Breads and cereals[e] | 0.09 (0.0, 0.3) | 7.2 (2, 26) | 0.26 (0.1, 0.4) | 23 (10, 35) | 0.2 (0.1, 0.2) | **<0.001** |
| Red meat[f] | 0.01 (0.0, 0.2) | 1.9 (0, 14) | 0.06 (0.0, 0.2) | 7.2 (1, 16) | 0.1 (0.0, 0.1) | **0.010** |
| Miscellaneous[g] | 0.01 (0.0, 0.1) | 1.1 (0, 6) | 0.01 (0.0, 0.1) | 1.3 (0, 6) | 0.0 (-0.0, 0.0) | 0.75 |
| Dairy | 0.00[i] (0.0, 0.0) | 0.1 (0, 0.4) | 0.00 (0.0, 0.0) | 0.5 (0, 2) | 0.0 (0.0, 0.0) | **0.010** |
| Legumes, nuts, seeds and eggs | 0.00 (0.0, 0.0) | 0.0 (0, 2) | 0.04 (0.0, 0.1) | 4.5 (1, 11) | 0.0 (0.0, 0.1) | **0.001** |
| Other meat[h] | 0.00 (0.0, 0.0) | 0.0 (0, 3) | 0.00 (0.0, 0.0) | 0.4 (0, 4) | 0.0 (-0.0, 0.0) | 0.57 |
| **12 months of age** | n=68 | | n=75 | | | |
| Breads and cereals[e] | 0.84 (0.5, 1.6) | 32 (16, 48) | 1.10 (0.6, 1.8) | 38 (27, 50) | 0.2 (-0.2, 0.5) | 0.26 |
| Vegetables | 0.38 (0.2, 0.5) | 11 (6, 16) | 0.29 (0.1, 0.5) | 8.9 (4, 14) | -0.1 (-0.2, -0.0) | **0.027** |
| Miscellaneous[g] | 0.32 (0.1, 0.6) | 9.8 (4, 18) | 0.18 (0.1, 0.5) | 5.7 (2, 17) | -0.1 (-0.3, 0.0) | 0.05 |
| Fruit and fruit juice | 0.27 (0.2, 0.5) | 8.3 (5, 13) | 0.32 (0.2, 0.5) | 10 (5, 14) | 0.0 (-0.1, 0.1) | 0.33 |
| Other meat[h] | 0.17 (0.1, 0.3) | 5.5 (2, 9) | 0.17 (0.1, 0.3) | 5.1 (1, 4) | -0.0 (-0.1, 0.1) | 0.94 |
| Legumes, nuts, seeds and eggs | 0.10 (0.0, 0.3) | 2.8 (0, 10) | 0.16 (0.0, 0.4) | 4.6 (1, 10) | 0.0 (-0.0, 0.1) | 0.28 |
| Red meat[f] | 0.09 (0.0, 0.3) | 2.5 (0, 11) | 0.15 (0.0, 0.4) | 3.8 (0, 12) | 0.1 (-0.1, 0.2) | 0.40 |
| Dairy | 0.06 (0.0, 0.1) | 1.5 (1, 4) | 0.05 (0.0, 0.1) | 1.7 (0, 4) | -0.0 (-0.0, 0.0) | 0.81 |
| Iron-fortified infant cereal | 0.00 (0.0, 0.0) | 0.0 (0, 0) | 0.00 (0.0, 0.1) | 0.0 (0, 5) | - | - |

**Bold** indicates a statistically significant difference at $p<0.05$

For peer review only

Data presented as median (25th, 75th percentile)

[a]Intake reported during the three-day weighed diet records collected at 7 and 12 months of age

[b]Ordered from highest to lowest contributor of iron to the intakes of the Control group

[c]Data expressed as median percentages (NB: *mean* percentages added to 100% of total iron intakes from complementary foods)

[d]Difference in median iron (mg/day) intake between groups: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control, adjusted for infant age and sex, and maternal education and parity

[e]Breads and cereals other than iron-fortified infant cereals

[f]Red meat defined as: beef, lamb, mutton, venison

[g]Miscellaneous defined as: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.

[h]Other meat defined as: fish, poultry, pork, processed meats

[i]Where the median intake is 0.00 this has occurred because more than half of the infants did not consume this food. Some infants did consume these foods, however, so it was possible for differences in intake to be significant. Similarly, the difference is reported as 0.00 if it is smaller than 0.05 and therefore rounds down to 0.00.

For peer review only

**Table 4** Iron status indicators and categories at 12 months of age

| | Control (n=59) | BLISS (n=60) | Difference (95% CI)[a] | *p* Value |
|---|---|---|---|---|
| Haemoglobin (g/L), mean (SD) | 117 (8.4) | 116 (8.9) | -0.8 (-4.0, 2.3) | 0.59 |
| Plasma ferritin (µg/L)[b] | 28.9 (18.5, 47.4) | 27.0 (19.5, 42.1) | -2.6 (-10.9, 5.8) | 0.55 |
| Soluble transferrin receptor (mg/L), mean (SD) | 7.6 (2.0) | 7.4 (2.7) | -0.2 (-1.0, 0.7) | 0.70 |
| Body iron (mg/kg)[c], mean (SD) | 3.3 (3.1) | 3.3 (2.9) | 0.04 (-1.1, 1.2) | 0.95 |
| C-reactive protein (mg/L) | 0.1 (0.0, 0.5) | 0.2 (0.1, 0.5) | -0.02 (-0.2, 0.2) | 0.86 |
| $\alpha_1$-acid glycoprotein (g/L) | 0.6 (0.4, 0.8) | 0.6 (0.5, 0.95) | 0.04 (-0.1, 0.2) | 0.56 |
| **Iron status categories, n (%)** | | | **OR (95% CI)[d]** | ***p* Value** |
| Iron sufficient[e] | 49 (83) | 50 (83) | 1.0 | - |
| Iron depleted[f] | 3 (5) | 2 (3) | 1.5 (0.2, 9.6) | 0.65 |
| Early functional iron deficiency[g] | 4 (7) | 4 (7) | 1.0 (0.2, 4.3) | 0.98 |
| Iron deficiency anaemia[h] | 3 (5) | 4 (7) | 0.8 (0.2, 3.6) | 0.74 |

Data presented as median (25th, 75th percentile), unless otherwise stated

[a]Difference adjusted for infant age and sex, and maternal education and parity: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control

[b]Ferritin adjusted for inflammation using multipliers proposed by *Thurnham et al*.[21]

[c]Body iron calculation (mg/kg) = -[log10(sTfR x 1000/ferritin) -2.8229]/0.1207 from *Cogswell et al.*[22]

[d]Odds ratio of Control relative to BLISS

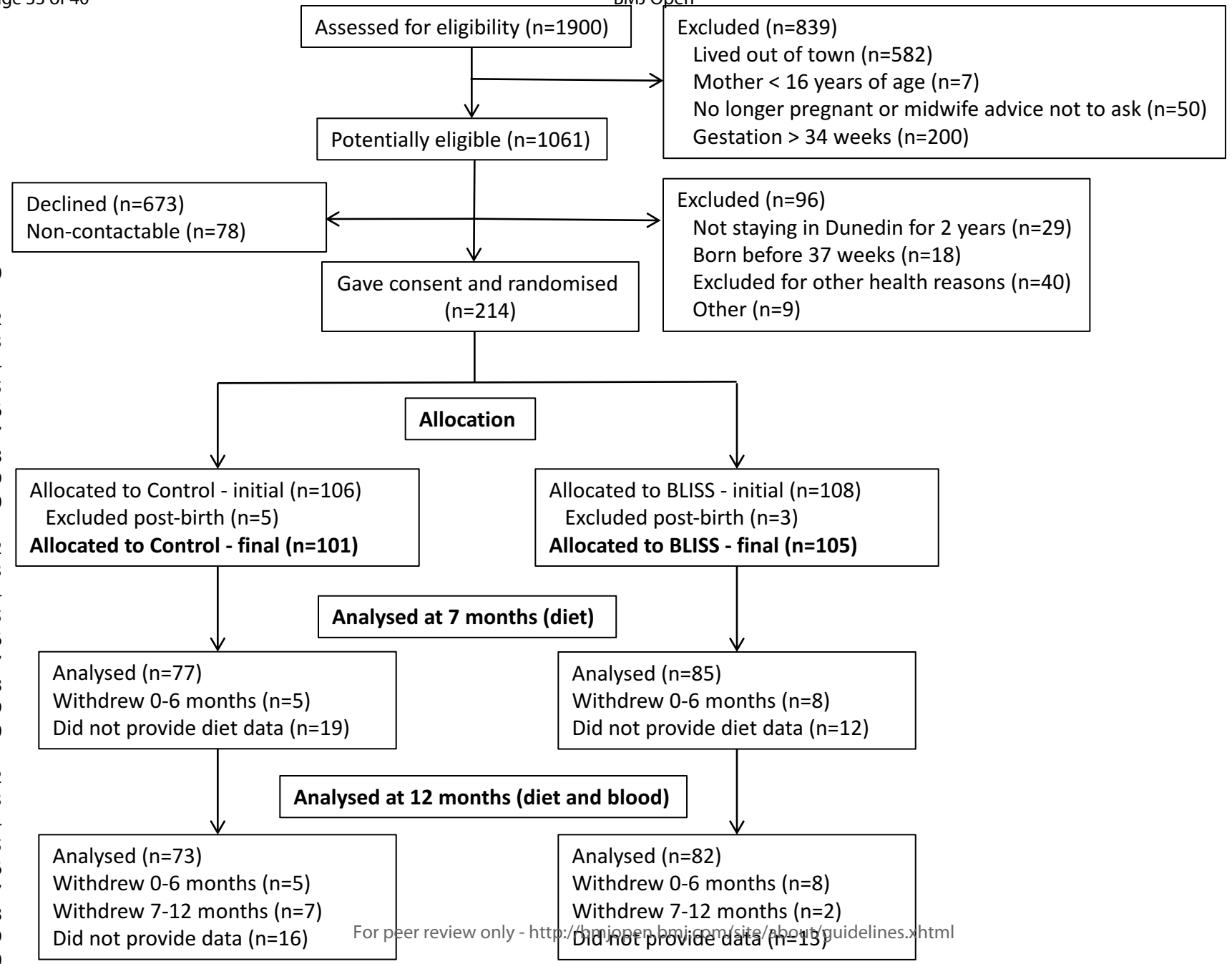
[e]Defined as body iron ≥0 mg/kg, haemoglobin ≥110 g/L and plasma ferritin ≥15 µg/L

[f]Defined as plasma ferritin <15 µg/L, in the absence of early functional iron deficiency and iron deficiency anaemia

[g]Defined as body iron <0 mg/kg and haemoglobin ≥110 g/L

[h]Defined as body iron <0 mg/kg and haemoglobin <110 g/L

For peer review only




For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

## Supplemental Tables

**eTable 1** Milk consumers at 7 and 12 months of age

**eTable 2** Number of consumers of each food group at 7 months of age

**eTable 3** Dietary sources of iron for consumers only at 7 months of age (complementary foods and infant milks)

**eTable 4** Number of consumers of each food group at 12 months of age

**eTable 5** Dietary sources of iron for consumers only at 12 months of age (complementary foods and infant milks)

For peer review only

**eTable 1** Milk consumers at 7 and 12 months of age[a,b]

| | Total | Control | BLISS | *p* Value |
|---|---|---|---|---|
| **7 months of age** | n=162 | n=77 | n=85 | |
| Breast milk only | 82 (51) | 38 (49) | 44 (52) | 0.95 |
| Infant formula only | 39 (24) | 19 (25) | 20 (23) | |
| Mixed (breast milk and infant formula) | 41 (25) | 20 (26) | 21 (25) | |
| **12 months of age** | n=143 | n=68 | n=75 | |
| Breast milk only | 62 (43) | 31 (46) | 31 (41) | 0.94 |
| Infant formula only | 47 (33) | 22 (32) | 25 (33) | |
| Mixed (breast milk and infant formula) | 15 (11) | 7 (10) | 8 (11) | |
| None of the above | 19 (13) | 8 (12) | 11 (15) | |
| Cow's milk[c] | | | | |
| None | 92 (64) | 47 (69) | 45 (60) | 0.51 |
| < 500mL/day | 40 (28) | 17 (25) | 23 (31) | |
| ≥ 500mL/day | 11 (8) | 4 (6) | 7 (9) | |

[a]Data presented as n (%)
[b]Based on intake reported during the three-day weighed diet records, collected at 7 and 12 months of age
[c]Cow's milk consumed as a drink

For peer review only

**eTable 2** Number of consumers of each food group at 7 months of age[a,b,c]

| | Control | BLISS | *p* Value |
|---|---|---|---|
| Breads and cereals[d] | 77 (100) | 85 (100) | - |
| Miscellaneous[e] | 77 (100) | 85 (100) | - |
| Vegetables | 75 (97) | 84 (99) | 0.50 |
| Fruit and fruit juice | 73 (95) | 81 (95) | 0.89 |
| Dairy | 66 (86) | 82 (96) | **0.015** |
| Breast milk | 58 (75) | 65 (76) | 0.87 |
| Red meat[f] | 42 (55) | 65 (76) | **0.003** |
| Iron-fortified infant cereal | 39 (51) | 62 (73) | **0.003** |
| Infant formula | 39 (51) | 41 (48) | 0.76 |
| Other meat[g] | 38 (49) | 45 (53) | 0.65 |
| Legumes, nuts, seeds and eggs | 26 (34) | 71 (84) | **<0.001** |

[a]Data presented as n (%)
[b]Intake reported during the three-day weighed diet records collected at 7 months of age
[c]Ordered by number of consumers in the Control group from highest to lowest
[d]Breads and cereals other than iron-fortified infant cereals
[e]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.
[f]Red meat defined as: beef, lamb, mutton, venison
[g]Other meat defined as: fish, poultry, pork, processed meats

For peer review only

**eTable 3** Dietary sources of iron for consumers only[a] at 7 months of age (complementary foods and infant milks)[b,c,d]

| | Control | | BLISS | | Difference (95% CI)[e] | *p* Value |
|---|---|---|---|---|---|---|
| | g/day | mg/day | g/day | mg/day | | |
| Infant formula | 309 (110, 745) | 5.5 (1.2, 8.3) | 525 (136, 804) | 6.0 (2.7, 7.5) | 0.5 (-2.0, 3.0) | 0.70 |
| Iron-fortified infant cereal | 4.0 (2, 9) | 0.72 (0.3, 1.3) | 1.7 (0.5, 5) | 0.37 (0.1, 0.9) | -0.3 (-0.7, -0.0) | **0.041** |
| Breast milk | 750 (660, 750) | 0.52 (0.46, 0.53) | 750 (660, 750) | 0.52 (0.48, 0.53) | 0.0 (-0.0, 0.0) | 0.99 |
| Vegetables | 34.8 (12, 72) | 0.16 (0.1, 0.4) | 20.5 (10, 43) | 0.10 (0.0, 0.2) | -0.06 (-0.1, 0.0) | 0.06 |
| Fruit and fruit juice | 55.6 (19, 94) | 0.14 (0.1, 0.3) | 39.5 (16, 69) | 0.10 (0.0, 0.2) | -0.0 (-0.1, 0.0) | 0.21 |
| Red meat[f] | 3.8 (1, 9) | 0.13 (0.0, 0.4) | 3.2 (1, 6) | 0.11 (0.0, 0.2) | -0.0 (-0.1, 0.1) | 0.50 |
| Breads and cereals[g] | 7.8 (2, 18) | 0.11 (0.0, 0.3) | 15.5 (8, 28) | 0.26 (0.1, 0.4) | 0.15 (0.1, 0.2) | **<0.001** |
| Legumes, nuts, seeds and eggs | 3.7 (1, 7) | 0.06 (0.01, 0.2) | 3.1 (1, 9) | 0.05 (0.0, 0.2) | -0.0 (-0.1, 0.0) | 0.41 |
| Other meat[h] | 3.6 (2, 8) | 0.04 (0.01, 0.1) | 4.7 (2, 9) | 0.04 (0.02, 0.1) | 0.0 (-0.0, 0.0) | 0.90 |
| Miscellaneous[i] | 40.0 (10, 85) | 0.01 (0.0, 0.1) | 32.8 (10, 61) | 0.02 (0.0, 0.1) | -0.0 (-0.0, 0.0) | 0.99 |
| Dairy | 10.8 (0.4, 29) | 0.0 (0.0, 0.0) | 9.4 (2, 24) | 0.0 (0.0, 0.0) | 0.0 (-0.0, 0.0) | 0.27 |

[a]Refer to eTable 2 for the number of consumers of each food group at 7 months of age
[b]Data presented as median (25$^{th}$, 75$^{th}$ percentile)
[c]Intake reported during the three-day weighed diet records collected at 7 months of age
[d]Ordered from highest to lowest food group contributing to total iron intakes in the Control group
[e]Difference in median iron (mg/day) intake between groups: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control
[f]Red meat defined as: beef, lamb, mutton, venison
[g]Breads and cereals other than iron-fortified infant cereals
[h]Other meat defined as: fish, poultry, pork and processed meats
[i]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.

For peer review only

5

**eTable 4** Number of consumers of each food group at 12 months of age[a,b,c]

| | Control | BLISS | *p* Value |
|---|---|---|---|
| Breads and cereals[d] | 68 (100) | 75 (100) | - |
| Miscellaneous[e] | 68 (100) | 75 (100) | - |
| Dairy | 68 (100) | 74 (99) | 0.34 |
| Vegetables | 67 (99) | 75 (100) | 0.29 |
| Fruit and fruit juice | 66 (97) | 72 (96) | 0.73 |
| Other meat[f] | 57 (84) | 67 (89) | 0.33 |
| Legumes, nuts, seeds and eggs | 55 (81) | 66 (88) | 0.24 |
| Red meat[g] | 41 (60) | 53 (71) | 0.19 |
| Breast milk | 38 (56) | 39 (52) | 0.64 |
| Infant formula | 29 (43) | 33 (44) | 0.87 |
| Iron-fortified infant cereal | 14 (21) | 21 (28) | 0.30 |

[a]Data presented as n (%)
[b]Intake reported during the three-day weighed diet records collected at 12 months of age
[c]Ordered by number of consumers in the Control group from highest to lowest
[d]Breads and cereals other than iron-fortified infant cereals
[e]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.
[f]Other meat defined as: fish, poultry, pork, processed meats
[g]Red meat defined as: beef, lamb, mutton, venison

For peer review only

**eTable 5** Dietary sources of iron for consumers only[a] at 12 months of age (complementary foods and infant milks)[b,c,d]

| | Control | | BLISS | | Difference (95% CI)[e] | *p* Value |
|---|---|---|---|---|---|---|
| | g/day | mg/day | g/day | mg/day | | |
| Infant formula | 414 (274, 569) | 4.9 (3.5, 6.4) | 329 (87, 524) | 3.8 (1.5, 5.4) | -1.1 (-2.9, 0.7) | 0.23 |
| Iron-fortified infant cereal | 7.2 (3, 15) | 1.2 (0.6, 3.5) | 3.3 (2, 5) | 0.73 (0.4, 1.2) | -0.7 (-1.8, 0.4) | 0.22 |
| Breads and cereals[f] | 57.1 (39, 74) | 0.84 (0.5, 1.6) | 60.2 (47, 82) | 1.10 (0.6, 1.8) | 0.2 (-0.2, 0.5) | 0.26 |
| Vegetables | 64.6 (45, 97) | 0.39 (0.2, 0.5) | 55.5 (26, 73) | 0.29 (0.1, 0.5) | -0.1 (-0.2, -0.0) | **0.023** |
| Miscellaneous[g] | 132 (89, 205) | 0.32 (0.1, 0.6) | 119 (67, 235) | 0.18 (0.1, 0.5) | -0.1 (-0.3, 0.0) | 0.05 |
| Breast milk | 448 (448, 448) | 0.31 (0.3, 0.31) | 448 (443, 448) | 0.31 (0.3, 0.31) | -0.0 (-0.0, 0.0) | 0.54 |
| Fruit and fruit juice | 94.4 (52, 132) | 0.27 (0.2, 0.5) | 106 (60, 165) | 0.32 (0.2, 0.5) | 0.1 (-0.0, 0.2) | 0.31 |
| Red meat[h] | 9.2 (5, 19) | 0.27 (0.1, 0.6) | 9.4 (4, 15) | 0.28 (0.1, 0.5) | 0.0 (-0.2, 0.2) | 0.89 |
| Other meal[i] | 17.7 (8, 28) | 0.21 (0.1, 0.3) | 15.7 (8, 27) | 0.19 (0.1, 0.3) | -0.0 (-0.1, 0.1) | 0.64 |
| Legumes, nuts, seeds and eggs | 7.2 (3, 25) | 0.14 (0.0, 0.4) | 11.2 (5, 23) | 0.20 (0.1, 0.4) | 0.1 (-0.0, 0.2) | 0.27 |
| Dairy | 84.4 (34, 188) | 0.06 (0.0, 0.1) | 109 (51, 188) | 0.06 (0.0, 0.1) | 0.0 (-0.0, 0.0) | 0.82 |

[a]Refer to eTable 4 for the number of consumers of each food group at 12 months of age
[b]Data presented as median (25$^{th}$, 75$^{th}$ percentile)
[c]Intake reported during the three-day weighed diet records collected at 12 months of age
[d]Ordered from highest to lowest food group contributing to total iron intakes in the Control group
[e]Difference in median iron (mg/day) intake between groups: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control
[f]Breads and cereals other than iron-fortified infant cereals
[g]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.
[h]Red meat defined as: beef, lamb, mutton, venison
[i]Other meat defined as: fish, poultry, pork, processed meats

For peer review only

## Checklist of items to include when reporting a randomized trial (56-58)

| PAPER SECTION<br>And topic | Item | Description | Reported on page # |
|---|---|---|---|
| *TITLE & ABSTRACT* | 1 | How participants were allocated to interventions (*e.g.*, "random allocation", "randomized", or "randomly assigned"). | 1, 5 |
| *INTRODUCTION*<br>Background | 2 | Scientific background and explanation of rationale. | 7 |
| *METHODS*<br>Participants | 3 | Eligibility criteria for participants and the settings and locations where the data were collected. | 8 |
| Interventions | 4 | Precise details of the interventions intended for each group and how and when they were actually administered. | 8-9 |
| Objectives | 5 | Specific objectives and hypotheses. | 7 |
| Outcomes | 6 | Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors). | 7 |
| Sample size | 7 | How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules. | 12 |
| Randomization --<br>Sequence generation | 8 | Method used to generate the random allocation sequence, including details of any restriction (*e.g.*, blocking, stratification). | 8 |
| Randomization --<br>Allocation concealment | 9 | Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned. | 8 |
| Randomization --<br>Implementation | 10 | Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups. | 8 |
| Blinding (masking) | 11 | Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. When relevant, how the success of blinding was evaluated. | 10 |
| Statistical methods | 12 | Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses. | 12-13 |
| RESULTS<br><br>Participant flow | 13 | Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons. | Figure 1 |
| Recruitment | 14 | Dates defining the periods of recruitment and follow-up. | 8, Figure 1 |
| Baseline data | 15 | Baseline demographic and clinical characteristics of each group. | Table 1 |
| Numbers analyzed | 16 | Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat" . State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%). | 12, tables |
| Outcomes and estimation | 17 | For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval). | 13-15 |
| Ancillary analyses | 18 | Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory. | 13-15 |
| Adverse events | 19 | All important adverse events or side effects in each intervention group. | 12 |
| DISCUSSION<br>Interpretation | 20 | Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes. | 15-18 |
| Generalizability | 21 | Generalizability (external validity) of the trial findings. | 15-18 |
| Overall evidence | 22 | General interpretation of the results in the context of current evidence. | 15-18 |

For peer review only

BMJ Open

# Impact of a modified version of Baby-Led Weaning on iron intake and status: a randomised controlled trial

| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2017-019036.R1 |
| Article Type: | Research |
| Date Submitted by the Author: | 21-Dec-2017 |
| Complete List of Authors: | Daniels, Lisa; University of Otago, Human Nutrition; University of Otago, Medicine<br>Taylor, Rachael; University of Otago, Medicine<br>Williams, Sheila; University of Otago, Preventive and Social Medicine<br>Gibson, R; University of Otago, Human Nutrition<br>Fleming, Elizabeth; University of Otago, Human Nutrition; University of Otago, Medicine<br>Wheeler, Benjamin; University of Otago, Women's and Children's Health<br>Taylor, Barry; University of Otago, Women's and Children's Health<br>Haszard, Jillian; University of Otago, Human Nutrition<br>Heath, Anne-Louise; University of Otago, Human Nutrition |
| Primary Subject Heading: | Nutrition and metabolism |
| Secondary Subject Heading: | Paediatrics, Public health |
| Keywords: | Baby-led weaning, Complementary feeding, Dietary iron, Iron status, Iron deficiency, Infants |
| | |

SCHOLARONE™
Manuscripts

# Impact of a modified version of Baby-Led Weaning on iron intake and status: a randomised controlled trial

Lisa Daniels, PhD[1,2]

Rachael W Taylor, PhD[2]

Sheila M Williams, DSc[3]

Rosalind S Gibson, PhD[1]

Elizabeth A Fleming, MCapSci[1,2]

Benjamin J Wheeler, FRACP[4]

Barry J Taylor, FRACP[4]

Jillian J Haszard, PhD[1]

*Anne-Louise M Heath, PhD[1]

[1]Department of Human Nutrition, University of Otago, PO Box 56, Dunedin 9054, New Zealand

[2]Department of Medicine, University of Otago, PO Box 56, Dunedin 9054, New Zealand

[3]Department of Preventive and Social Medicine, University of Otago, PO Box 56, Dunedin 9054, New Zealand

[4]Department of Women's and Children's Health, University of Otago, PO Box 56, Dunedin 9054, New Zealand

*** Corresponding author**

Anne-Louise M Heath

Department of Human Nutrition

For peer review only

University of Otago

PO Box 56

Dunedin 9054

New Zealand

Telephone: +64 3 479 8379

Email: anne-louise.heath@otago.ac.nz

**Funding statement:** This work was supported by Meat & Livestock Australia, Lottery Health Research, Karitane Products Society, Perpetual Trustees, the University of Otago, and the New Zealand Federation of Women's Institutes. The funders provided funds only and played no role in the study design, development of the study aims, carrying out the study or the analysis, or interpretation of the results. Heinz Wattie's Limited provided baby rice cereal for participants in the intervention group. Part of Professor R Taylor's salary is from a Karitane Products Society (KPS) Fellowship that is paid via the University of Otago. Dr L Daniels was supported by a University of Otago Doctoral Scholarship, and a University of Otago Postgraduate Publishing Bursary.

**Competing interests statement:** We have read and understood the BMJ policy on declaration of interests and declare that we have no competing interests.

**Clinical Trial Registration:** Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au). Identifier ACTRN12612001133820.

**Data Sharing Statement:** No additional data are available.

**Abbreviations**

For peer review only

| | |
|---|---|
| AGP | $\alpha_1$-acid glycoprotein |
| BLW | Baby-Led Weaning |
| BLISS | Baby-Led Introduction to SolidS |
| CRP | C-reactive protein |
| EFSA | European Food Safety Authority |
| GP | general practitioner |
| MFP | 'meat, fish, poultry' |
| sTfR | soluble transferrin receptor |
| WDR | weighed three-day diet record |

**Abstract word count:** 282

**Word count:** 4,509

For peer review only

**Abstract**

**Objective:** To determine the iron intake and status of infants following a version of Baby-Led Weaning (BLW) modified to prevent iron deficiency (Baby-Led Introduction to SolidS; BLISS) compared to those of infants following traditional spoon-feeding.

**Design, participants and intervention:** This randomised controlled trial included 206 participants assigned to Control (n=101) or BLISS (n=105) groups. Both groups received standard midwifery and 'Well Child' care. BLISS participants received eight additional visits (from before birth to 9 months) providing education and support on the BLISS approach to complementary feeding (i.e. BLW modified to increase iron intake). The primary outcome of the BLISS study (growth) has been previously reported. This paper reports the key pre-specified secondary outcomes iron intake and iron status.

**Outcome measures:** Intake of iron and key absorption modifiers was assessed using weighed three-day diet records at 7 and 12 months. A venipuncture blood sample was collected at 12 months to determine plasma ferritin, haemoglobin, soluble transferrin receptor, C-reactive protein, and $\alpha_1$-acid glycoprotein concentrations; and body iron was calculated.

**Results:** Differences in median dietary iron intakes between the Control and BLISS groups were not significant at 7 (difference 0.6 mg/day; 95% CI: -1.0 to 2.3) or 12 (-0.1 mg/day; -1.6 to 1.4) months of age. Similarly, there were no significant differences in plasma ferritin concentration (difference -2.6 µg/L; 95% CI: -10.9 to 5.8), body iron (0.04 mg/kg; -1.1 to 1.2), or the prevalence of depleted iron stores, early functional iron deficiency, or iron deficiency anaemia (all $p \geq 0.65$) at 12 months of age.

**Conclusions:** A baby-led approach to complementary feeding does not appear to increase the risk of iron deficiency in infants when their parents are given advice to offer 'high-iron' foods with each meal.

For peer review only

**Trial registration:** Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au). Identifier ACTRN12612001133820.

**Keywords:** Baby-led weaning, complementary feeding, dietary iron, iron status, iron deficiency, body iron, infants, toddlers

For peer review only

## Article summary

### Strengths and limitations of this study:

- First randomised controlled trial to investigate the impact of a baby-led approach to complementary feeding on iron intake and biochemical iron status.
- Robust dietary assessment data provided by weighed diet records collected on non-consecutive days.
- Did not reach planned sample size, but confidence intervals are provided to indicate the range of plausible values in the population.
- This trial cannot be used to draw conclusions about the risk of iron deficiency in infants following unmodified BLW.

For peer review only

## Introduction

Anecdotal reports suggest that many parents are following Baby-Led Weaning (BLW) with their infants, particularly in New Zealand,[1] the United Kingdom,[2] and Canada.[3] However, health professionals have expressed concerns about this alternative approach to complementary feeding that need to be addressed.[3,4] Infants following BLW are expected to feed themselves *all* of their food from the start of the complementary feeding period[5] and it has been proposed that this may increase the risk of iron deficiency if the majority of first foods offered are foods low in iron, such as fruits and vegetables, or if iron-fortified infant cereals are avoided due to their semi-liquid consistency.[6] A recent observational study reported that mean dietary iron intake in infants following BLW was less than half that of infants following traditional spoon-feeding.[6] However, the impact of this lower iron intake on the biochemical iron status of infants has not been examined in that[6] or any other study.

Iron deficiency that progresses to iron deficiency anaemia can impact on the central nervous system and development during infancy, leading to poorer cognitive and behavioural performance.[7] Moreover, these impacts on infant development may not be reversible.[8,9] It is important, therefore, to determine whether a baby-led approach can be followed without increasing the risk of iron deficiency before baby-led approaches can be considered an appropriate alternative to traditional complementary feeding practices.

The aim of the Baby-led Introduction to SolidS (BLISS) study was to determine whether a modified version of BLW prevents young children from becoming overweight,[10] without increasing their risk of iron deficiency, growth faltering,[10] and choking.[11] In this paper we report the key pre-specified secondary outcomes iron intake (at 7 and 12 months of age)

For peer review only

and iron status (at 12 months) of infants following BLISS compared with traditional spoon-feeding.

**Methods**

Detailed methods have been described elsewhere[12] so only relevant information is included here. The Lower South Regional Ethics Committee (LRS/11/09/037) approved the study and adult participants gave written informed consent. Pregnant women in their third trimester of pregnancy who were booked into the Queen Mary Maternity Hospital in Dunedin, New Zealand were invited into the study between November 2012 and March 2014. Delayed cord clamping was infrequently practiced in Queen Mary Maternity Hospital at the time of the study. Women were eligible if they: spoke English or Te Reo Māori (the indigenous language of New Zealand); planned to live in Dunedin, New Zealand, until their child was at least 2 years of age; and were 16 years of age or older. Women were excluded if their infant was born before 37 weeks gestation, or had a congenital abnormality, physical condition or intellectual disability that was likely to affect their feeding or growth. Participants were randomised using random length blocks after stratification for parity (first child, subsequent child) and maternal education (tertiary, non-tertiary), to Control (n=101) or BLISS (n=105) groups by the study biostatistician. The BLISS study, and intervention, are not in any way related to the UK-based Bliss charity for "babies born premature or sick" (www.bliss.org.uk).

**Intervention**

The Control group participants received routine midwifery (until 6 weeks of age) and 'Well Child' care (from 6 weeks). 'Well Child Tamariki Ora' is a nationally funded program to support and educate families with children under 5 years of age. The program recommends

For peer review only

exclusive breastfeeding until around 6 months of age with the introduction of complementary foods at around 6 months.[13]

Participants in the BLISS group received routine midwifery and 'Well Child' care, and BLISS support and education from before birth (approximately 34-35 weeks gestation) until 9 months of age. The BLISS approach was based on three key principles of BLW: exclusive milk feeding until 6 months of age, infant self-feeding from the start of complementary feeding (i.e. baby-led from 6 months of age), and offering family foods as finger foods so they can be picked up by the infant. However, BLISS also included modifications to address the three main concerns about BLW expressed by health professionals:[3,4] iron deficiency, growth faltering,[10] and choking.[11]

The BLISS intervention comprised: 1) five contacts with a lactation consultant (from the third trimester of pregnancy to 6 months of age) to encourage and support exclusive milk feeding (ideally breastfeeding) and delay the introduction of complementary foods until 6 months of age, 2) three contacts with BLISS research staff to give individualised advice on how to follow BLISS (at 5.5, 7 and 9 months of age), and 3) a range of written resources that were developed to help parents follow BLISS,[14] including recipe books given at 5.5, 7 and 9 months of age, and lists of age-appropriate foods.[12] Parents were encouraged to offer their child three types of finger foods at every meal: a 'high-iron' food (e.g., red meat, iron-fortified infant cereal (in a hand held way, e.g., on toast)), an energy rich food (>1.5 kcal/g, e.g., avocado, cheese), and an easy to eat food such as fruit or vegetables. BLISS participants were provided with complementary packets of iron-fortified infant cereal (For Baby Rice Cereal, Heinz Watties Ltd., Australia) at each of the intervention visits (5.5, 7, and 9 months).

For peer review only

The iron content of this infant cereal was 2.2 mg per 100 g of infant cereal prepared with water.

**Adherence**

Questionnaires were used to determine adherence to BLISS by asking parents 'how has your baby been fed solids in the past week?' when their infant was 7 and 12 months of age. Adherence to BLISS was defined as the infant feeding themselves most or all of their food in the past week.

**Outcome Assessment**

Demographic data were collected at baseline by questionnaire, except for birth weight and gestational age which were obtained from hospital records. Research staff conducting measurement visits and administering questionnaires were blinded to group allocation. At 2, 4, 6, 7, 8, 9 and 12 months of age brief feeding questionnaires were used to collect information including the age when breastfeeding stopped and/or formula feeding started and stopped.

***Dietary Assessment***

Weighed three-day diet records (WDRs) were used to assess dietary intake at 7 and 12 months of age. Parent participants were given detailed instructions and provided with dietary scales (Salter Electronic, Salter Housewares Ltd. Tonbridge, UK) accurate to ±1 g. They then recorded everything their child ate and drank over three randomly assigned non-consecutive days (two week days and one weekend day) over a three week period. Parents were asked to record the total weight of food offered, and to collect, weigh and record all leftover food including food on the floor, baby, or the tray, so that the amount of food consumed by the infant could be calculated. Any supplements consumed were also recorded.

For peer review only

The WDRs were entered into Kai-culator (Version 1.13s, University of Otago, New Zealand), a dietary analysis program that includes dietary data from the New Zealand Food Composition Database (FOODfiles 2010, Plant and Food Research),[15] commonly consumed recipes from the 2008/09 New Zealand Adult Nutrition Survey,[16] and commercial infant foods collated by the research team.[17] It was not possible to directly measure breast milk intake so it was assumed to be 750 g per day at 7 months and 448 g per day at 12 months based on a quadratic curve fitted to the breast milk volumes reported by Dewey et al.[18] If the infant was fed both breast milk and infant formula then the gram amount of infant formula consumed was subtracted from the estimated total breast milk intake (i.e. 750 or 448 g per day).The iron content of breast milk was assumed to be 0.07 mg per 100 g.[15]

Grams of red meat, grams of 'meat, fish, poultry' (MFP), milligrams of haem iron,[19] and milligrams of phytate[20] were determined using values from the literature and information from manufacturers.

***Biochemical Assessment***

A non-fasting venous blood sample was obtained from 119 infants at 12 months of age (58% of total study participants). Of those who did not provide a blood sample, 26 blood draws were unsuccessful, 22 had withdrawn from the study by 12 months of age, 13 could not be contacted or were living out of town, and 26 parents did not provide consent for the blood test. Blood samples were drawn from an antecubital vein into a trace element-free lithium heparin anticoagulated tube (7.5 mL; S-Monovette, Sarstedt, Nümbrecht, Germany) and refrigerated immediately after collection. If the child was unwell the blood test was delayed

For peer review only

for 14 days.

Complete blood count (Sysmex XE 5000, Kobe, Japan) and plasma ferritin (Cobas 8000 unit e 602, Roche, USA) were determined on collection day by Southern Community Laboratories Ltd., (Dunedin, New Zealand). Aliquots of plasma were stored at ˉ80°C until subsequent analysis of soluble transferrin receptor (sTfR), C-reactive protein (CRP), and $\alpha_1$-acid glycoprotein (AGP), using a Cobas C311 (Roche, USA) at the Department of Human Nutrition laboratories (University of Otago, Dunedin, New Zealand). Cutoffs of > 5 mg/L CRP and > 1 g/L AGP defined the presence of inflammation, for example as a result of infection. Ferritin multipliers were used to adjust ferritin concentrations to remove the influence of this inflammation.[21] The sTfR values were converted to be equivalent with the Flowers assay:[22] 1.5 x Roche sTfR + 0.35 mg/L and body iron (mg/kg) was calculated:[22] -[log10(sTfR x 1000/ferritin) -2.8229]/0.1207.

**Adverse Events**

Participants with biochemical results outside pre-defined clinical reference ranges for Complete Blood Count indices or plasma ferritin were contacted, informed of the abnormal result, and advised to visit their general practitioner for advice.

**Statistical Analysis**

The data were analysed according to modified intention to treat. A sample size of 84 participants per group provided 80% power ($\alpha$=0.05) to detect a difference in geometric mean plasma ferritin concentrations of 5.0 µg/L.[12]

For peer review only

The proportions of infants at 7 and 12 months of age fed breast milk, infant formula, or both ('mixed fed'), as well as those consuming cow's milk were determined using Chi-squared tests. All nutrient and food group data are presented as daily averages over the three days. As most variables were positively skewed, the data are reported as medians and lower and upper quartiles ($25^{th}$ and $75^{th}$). Quantile regression was used to estimate the difference between the Control and BLISS groups for energy and nutrient intake, as well as dietary iron intake from each food group. Usual iron intake was determined,[23] and the prevalence of inadequate iron intakes was estimated using the full-probability approach.[24]

Means and standard deviations are used to describe all of the biochemical variables except plasma ferritin, CRP and AGP, which are presented as medians and lower and upper quartiles. Differences in biochemical iron status indices were estimated using regression and were adjusted for infant age at the time of blood test, infant sex, maternal education (non tertiary vs tertiary) and maternal parity (1 child vs > 1 child, including the current pregnancy). A Chi-squared test was used to compare the number of cases and controls for each of the iron status categories, and their associated odds ratios.

All analyses were conducted using statistical software Stata, version 13 (StataCorp LP, Texas, USA).

**Results**

A total of 214 mother-infant pairs were randomised, of whom eight were excluded after birth (n=5 Control, n=3 BLISS), providing a final sample size of 206 participants (**Figure 1**). Of these 206 participants, 81 Control and 88 BLISS participants provided data for this secondary analysis (**Table 1**).

For peer review only

**Table 1** Characteristics of participants who provided intake data at 7 and/or 12 months of age or biochemical data at 12 months of age

| | Control (n=81) | BLISS (n=88) |
|---|---|---|
| **Maternal and household variables** | | |
| Maternal age at birth (years), mean (SD) | 32.2 (5.8) | 31.7 (4.8) |
| Maternal parity | | |
| First child | 32 (40) | 37 (42) |
| Two children | 27 (33) | 37 (42) |
| Three or more children | 22 (27) | 14 (16) |
| Maternal ethnicity | | |
| NZ European | 70 (87) | 71 (80) |
| Māori | 6 (7) | 8 (9) |
| Other | 5 (6) | 9 (10) |
| Maternal education | | |
| School only | 23 (28) | 26 (30) |
| Post-secondary | 13 (16) | 20 (22) |
| University | 45 (56) | 42 (48) |
| Household deprivation[a] | | |
| 1-3 (Low) | 24 (30) | 25 (28) |
| 4-7 | 37 (45) | 46 (53) |
| 8-10 (High) | 20 (25) | 17 (19) |
| **Infant variables** | | |
| Sex | | |
| Female | 37 (46) | 50 (57) |

For peer review only

| | | |
|---|---|---|
| Male | 44 (54) | 38 (43) |
| Infant birth weight (g), mean (SD) | 3510 (453) | 3496 (448) |
| Infant gestational age at birth (weeks), mean (SD) | 39.5 (1.2) | 39.7 (1.0) |
| **Complementary feeding variables** | | |
| Age complementary foods were introduced (weeks), mean (SD) | 22.6 (3.1) | 24.6 (3.2)[b] |
| Complementary foods delayed to 6 months of age | 15 (18) | 58 (66)[b] |

Abbreviation: NZ European; New Zealand European
Data presented as n (%), unless otherwise stated
[a]Household deprivation categorised using the NZDep2013 scale in which decile 1 indicates the lowest level of deprivation and 10 indicates the highest[25]
[b]$p<0.001$

For peer review only

Baseline demographic data, and age when complementary foods were introduced, are shown in Table 1. There were no differences in the characteristics of participants who were included in this analysis (i.e. provided either intake or status data) compared with those not included (i.e. provided neither intake nor status data) with the exception of maternal age at birth, which was lower for those who did not provide data (**eTable 1**).

Adherence to the baby-led approach was high in the BLISS group with significantly more infants feeding themselves most or all of their food in the past week at 7 (74% vs 19% Control; $p<0.001$) and 12 (77% vs 48% Control; $p<0.001$) months of age.

The differences in iron intake between the BLISS group and the Control group at 7 and 12 months were 0.6 mg/day (95% C: -1.0, 2.3) at 7 months and -0.1 mg/day (-1.6, 1.4) at 12 months (**Table 2**). In both cases the differences were small and the confidence intervals exclude clinically interesting differences. The same applies to intakes of the iron absorption modifiers that were measured, except for a significantly lower intake of Vitamin C in BLISS (49.2 mg/day) compared with Control infants (59.2 mg/day) at 7 months (adjusted difference -9.7 mg/day; 95% CI: -18.4 to -0.9) (Table 2). Four participants (n=2 BLISS, n=2 Control) were using iron supplements at the time of the 12-month WDR but these have not been included as the supplements were started after the blood sample was collected.

For peer review only

**Table 2** Intake of iron and key absorption modifiers at 7 and 12 months of age from complementary foods and infant milks[a]

| | Control | BLISS | Difference (95% CI)[b] | *p* Value |
|---|---|---|---|---|
| **7 months of age** | n=77 | n=85 | | |
| Energy (kJ/day), mean (SD) | 2862 (548) | 2996 (613) | 145 (-31.2, 321) | 0.11 |
| Energy from complementary foods only (kJ/day)[c], mean (SD) | 672 (506) | 799 (595) | 144 (-26.2, 314) | 0.10 |
| Dietary iron (mg/day) | 2.7 (1.3, 6.9) | 3.0 (1.5, 7.3) | 0.6 (-1.0, 2.3) | 0.46 |
| Dietary iron from complementary foods only (mg/day)[d] | 1.0 (0.5, 2.2) | 1.2 (0.7, 2.0) | 0.2 (-0.2, 0.6) | 0.34 |
| Haem iron (mg/day) | 0.0 (0.0, 0.1) | 0.0 (0.0, 0.1) | 0.0 (-0.0, 0.1) | 0.10 |
| Non-haem iron (mg/day) | 2.6 (1.3, 6.9) | 2.9 (1.4, 7.3) | 0.4 (-1.3, 2.0) | 0.67 |
| Meat, fish, poultry (g/day) | 2.8 (0.0, 11.1) | 4.3 (1.4, 8.8) | 1.3 (-1.9, 4.4) | 0.42 |
| Phytate (mg/day) | 36 (16.3, 75.2) | 45 (23.0, 77.6) | 4.2 (-15.0, 23.4) | 0.67 |
| Phytate:iron molar ratio[e] | 1.0 (0.4, 2.3) | 1.3 (0.6, 2.7) | 0.4 (-0.2, 1.0) | 0.18 |
| Vitamin C (mg/day) | 59.2 (41.7, 75.6) | 49.2 (38.3, 67.9) | -9.7 (-18.4, -0.9) | **0.032** |
| **12 months of age** | n=68 | n=75 | | |
| Energy (kJ/day), mean (SD) | 3573 (776) | 3623 (1048) | 109 (-191, 409) | 0.48 |
| Energy from complementary foods only (kJ/day)[c], mean (SD) | 2400 (848) | 2527 (1183) | 195 (-142, 533) | 0.25 |
| Dietary iron (mg/day) | 5.3 (3.1, 8.4) | 4.7 (3.1, 7.3) | -0.1 (-1.6, 1.4) | 0.87 |
| Dietary iron from complementary foods only (mg/day)[d] | 3.2 (2.3, 4.6) | 3.2 (2.5, 4.1) | -0.0 (-0.6, 0.6) | 0.94 |
| Haem iron (mg/day) | 0.2 (0.1, 0.3) | 0.2 (0.1, 0.3) | 0.0 (-0.0, 0.1) | 0.57 |
| Non-haem iron (mg/day) | 5.0 (2.9, 8.1) | 4.5 (2.9, 7.0) | -0.1 (-1.7, 1.4) | 0.85 |

For peer review only

| | | | | |
|---|---|---|---|---|
| Meat, fish, poultry (g/day) | 19.3 (7.9, 33.6) | 19.3 (11.2, 31.1) | -1.4 (-9.0, 6.2) | 0.72 |
| Phytate (mg/day) | 187 (118, 310) | 229 (152, 274) | 37 (-20.4, 94.8) | 0.20 |
| Phytate:iron molar ratio[e] | 3.8 (2.3, 6.2) | 4.3 (2.8, 6.5) | 0.6 (-0.7, 1.9) | 0.35 |
| Vitamin C (mg/day) | 48.1 (39.4, 69.5) | 50.4 (36.6, 61.4) | 0.4 (-9.4, 10.3) | 0.93 |

Data presented as median ($25^{th}$, $75^{th}$ percentile), unless otherwise stated

[a]Intake reported during the three-day weighed diet records collected at 7 and 12 months of age

[b]Difference adjusted for infant age (by day) and sex, and maternal education and parity

[c]Excludes energy from breast milk and infant formula

[d]Excludes iron from breast milk and infant formula

[e]Calculated as [phytate (mg) / 660] / [iron (mg) / 55.9]

For peer review only

There was no difference in the number of infants who were fed breast milk, formula or both, between groups at either 7 or 12 months (**eTable 2**). There were no significant differences in estimated breast milk or infant formula intake between groups at 7 (breast milk difference 0.0 g/day; 95% CI: -5.1 to 5.1; *p*=1.00; infant formula difference 216 g/day; -97.2 to 530; *p*=0.17) or 12 (breast milk difference 0.0 g/day; 95% CI: -0.1 to 0.1; *p*=0.94; infant formula difference -85 g/day; -277 to 107; *p*=0.38) months of age, and therefore no differences between groups in the contribution of infant milks to iron intake (all *p*>0.17).

BLISS infants obtained significantly more iron from 'breads and cereals', 'red meat', 'dairy', and 'legumes, nuts, seeds and eggs' than Control infants at 7 months of age (**Table 3**). For all these food groups, except 'breads and cereals', this reflected the greater proportion of BLISS infants consuming these foods (**eTable 3**). However, the differences in iron contribution were small (e.g., adjusted difference 0.1 mg iron/day from red meat; 95% CI: 0.01 to 0.1) in comparison to the Average Requirement of 5.0 mg/day[26] and therefore not likely to be clinically significant. None of the differences apparent at 7 months remained at 12 months, and although BLISS infants did receive significantly less iron from 'vegetables' than Control infants at 12 months, the actual difference was very small (-0.1 mg iron/day; 95% CI: -0.2 to -0.0) (Table 3).

For peer review only

**Table 3** Iron from complementary foods at 7 and 12 months of age (consumers and non-consumers)[a,b]

| | Control | | BLISS | | Difference (95% CI)[d] | *p* Value |
|---|---|---|---|---|---|---|
| | mg/day | %[c] | mg/day | %[c] | | |
| **7 months of age** | n=77 | | n=85 | | | |
| Vegetables | 0.16 (0.0, 0.4) | 17 (9, 25) | 0.10 (0.0, 0.2) | 8.4 (6, 17) | -0.1 (-0.1, 0.0) | 0.07 |
| Fruit and fruit juice | 0.13 (0.0, 0.2) | 11 (5, 24) | 0.09 (0.0, 0.2) | 7.2 (3, 12) | -0.0 (-0.1, 0.0) | 0.19 |
| Iron-fortified infant cereal | 0.08 (0.0, 0.7) | 7.9 (0, 54) | 0.19 (0.0, 0.5) | 19 (0, 43) | 0.1 (-0.1, 0.3) | 0.25 |
| Breads and cereals[e] | 0.09 (0.0, 0.3) | 7.2 (2, 26) | 0.26 (0.1, 0.4) | 23 (10, 35) | 0.2 (0.1, 0.2) | **<0.001** |
| Red meat[f] | 0.01 (0.0, 0.2) | 1.9 (0, 14) | 0.06 (0.0, 0.2) | 7.2 (1, 16) | 0.1 (0.0, 0.1) | **0.010** |
| Miscellaneous[g] | 0.01 (0.0, 0.1) | 1.1 (0, 6) | 0.01 (0.0, 0.1) | 1.3 (0, 6) | 0.0 (-0.0, 0.0) | 0.75 |
| Dairy | 0.00[i] (0.0, 0.0) | 0.1 (0, 0.4) | 0.00 (0.0, 0.0) | 0.5 (0, 2) | 0.0 (0.0, 0.0) | **0.010** |
| Legumes, nuts, seeds and eggs | 0.00 (0.0, 0.0) | 0.0 (0, 2) | 0.04 (0.0, 0.1) | 4.5 (1, 11) | 0.0 (0.0, 0.1) | **0.001** |
| Other meat[h] | 0.00 (0.0, 0.0) | 0.0 (0, 3) | 0.00 (0.0, 0.0) | 0.4 (0, 4) | 0.0 (-0.0, 0.0) | 0.57 |
| **12 months of age** | n=68 | | n=75 | | | |
| Breads and cereals[e] | 0.84 (0.5, 1.6) | 32 (16, 48) | 1.10 (0.6, 1.8) | 38 (27, 50) | 0.2 (-0.2, 0.5) | 0.26 |
| Vegetables | 0.38 (0.2, 0.5) | 11 (6, 16) | 0.29 (0.1, 0.5) | 8.9 (4, 14) | -0.1 (-0.2, -0.0) | **0.027** |
| Miscellaneous[g] | 0.32 (0.1, 0.6) | 9.8 (4, 18) | 0.18 (0.1, 0.5) | 5.7 (2, 17) | -0.1 (-0.3, 0.0) | 0.05 |
| Fruit and fruit juice | 0.27 (0.2, 0.5) | 8.3 (5, 13) | 0.32 (0.2, 0.5) | 10 (5, 14) | 0.0 (-0.1, 0.1) | 0.33 |
| Other meat[h] | 0.17 (0.1, 0.3) | 5.5 (2, 9) | 0.17 (0.1, 0.3) | 5.1 (1, 4) | -0.0 (-0.1, 0.1) | 0.94 |
| Legumes, nuts, seeds and eggs | 0.10 (0.0, 0.3) | 2.8 (0, 10) | 0.16 (0.0, 0.4) | 4.6 (1, 10) | 0.0 (-0.0, 0.1) | 0.28 |
| Red meat[f] | 0.09 (0.0, 0.3) | 2.5 (0, 11) | 0.15 (0.0, 0.4) | 3.8 (0, 12) | 0.1 (-0.1, 0.2) | 0.40 |
| Dairy | 0.06 (0.0, 0.1) | 1.5 (1, 4) | 0.05 (0.0, 0.1) | 1.7 (0, 4) | -0.0 (-0.0, 0.0) | 0.81 |
| Iron-fortified infant cereal | 0.00 (0.0, 0.0) | 0.0 (0, 0) | 0.00 (0.0, 0.1) | 0.0 (0, 5) | - | - |

**Bold** indicates a statistically significant difference at $p<0.05$

For peer review only

Data presented as median (25th, 75th percentile)

[a]Intake reported during the three-day weighed diet records collected at 7 and 12 months of age

[b]Ordered from highest to lowest contributor of iron to the intakes of the Control group

[c]Data expressed as median percentages (NB: *mean* percentages added to 100% of total iron intakes from complementary foods)

[d]Difference in median iron (mg/day) intake between groups: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control, adjusted for infant age (by day) and sex, and maternal education and parity

[e]Breads and cereals other than iron-fortified infant cereals

[f]Red meat defined as: beef, lamb, mutton, venison

[g]Miscellaneous defined as: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.

[h]Other meat defined as: fish, poultry, pork, processed meats

[i]Where the median intake is 0.00 this has occurred because more than half of the infants did not consume this food. Some infants did consume these foods, however, so it was possible for differences in intake to be significant. Similarly, the difference is reported as 0.00 if it is smaller than 0.05 and therefore rounds down to 0.00.

For peer review only

BLISS specifically encouraged consumption of 'high-iron' foods such as red meat and iron-fortified infant cereal from the start of complementary feeding. BLISS infants were introduced to 'red meat' at the same age as Control infants (28.1 weeks, 27.9 weeks, $p$=0.74). Although significantly more BLISS than Control infants consumed 'red meat' at 7 months of age (76%, 55%; eTable 3), intakes were similarly low for consumers in both groups (BLISS 3.2 g/day, Control 3.8 g/day; **eTable 4**). BLISS infants began consuming 'iron-fortified infant cereal' approximately two weeks later than Control infants (25.4 weeks, 23.7 weeks, $p$=0.008). Interestingly, more BLISS infants were consuming 'iron-fortified infant cereal' by 7 months of age (73%, 51% Control) (eTable 3), but the median amounts consumed were very small (BLISS 1.7 g/day, Control 4.0 g/day) (eTable 4). At 12 months there were no significant differences in the number of consumers of 'iron-fortified infant cereal' or 'red meat', or in the amount consumed (**eTables 5 and 6**).

The prevalence of inadequate iron intakes was high at 74% for both groups at 7 months of age, but considerably lower by 12 months (23% Control, 26% BLISS).

The difference between the BLISS and Control groups for plasma ferritin was -2.6 µg/L (-10.9, 5.8), and not statistically significant, although the lower confidence limit does suggest it is plausible that BLISS infants as a population could have plasma ferritin concentrations that are 11 µg/L lower than those of Control infants. Differences between the groups for the other biochemical indicators of iron status were small and not statistically significant (all $p$>0.55) (**Table 4**). Few participants had signs of inflammation/infection (n=8 Control, n=11 BLISS). The majority of infants in both groups were iron sufficient (83% Control, 83% BLISS), although 5% Control and 7% BLISS presented with iron deficiency anaemia (Table 4).

For peer review only

**Table 4** Iron status indicators and categories at 12 months of age

| | Control (n=59) | BLISS (n=60) | Difference (95% CI)[a] | *p* Value |
|---|---|---|---|---|
| Haemoglobin (g/L), mean (SD) | 117 (8.4) | 116 (8.9) | -0.8 (-4.0, 2.3) | 0.59 |
| Plasma ferritin (µg/L)[b] | 28.9 (18.5, 47.4) | 27.0 (19.5, 42.1) | -2.6 (-10.9, 5.8) | 0.55 |
| Soluble transferrin receptor (mg/L), mean (SD) | 7.6 (2.0) | 7.4 (2.7) | -0.2 (-1.0, 0.7) | 0.70 |
| Body iron (mg/kg)[c], mean (SD) | 3.3 (3.1) | 3.3 (2.9) | 0.04 (-1.1, 1.2) | 0.95 |
| C-reactive protein (mg/L) | 0.1 (0.0, 0.5) | 0.2 (0.1, 0.5) | -0.02 (-0.2, 0.2) | 0.86 |
| $\alpha_1$-acid glycoprotein (g/L) | 0.6 (0.4, 0.8) | 0.6 (0.5, 0.95) | 0.04 (-0.1, 0.2) | 0.56 |
| **Iron status categories, n (%)** | | | **OR (95% CI)[d]** | ***p* Value** |
| Iron sufficient[e] | 49 (83) | 50 (83) | 1.0 | - |
| Iron depleted[f] | 3 (5) | 2 (3) | 1.5 (0.2, 9.6) | 0.65 |
| Early functional iron deficiency[g] | 4 (7) | 4 (7) | 1.0 (0.2, 4.3) | 0.98 |
| Iron deficiency anaemia[h] | 3 (5) | 4 (7) | 0.8 (0.2, 3.6) | 0.74 |

Data presented as median (25th, 75th percentile), unless otherwise stated

[a]Difference adjusted for infant age (by day) and sex, and maternal education and parity: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control

[b]Ferritin adjusted for inflammation using multipliers proposed by *Thurnham et al*.[21]

[c]Body iron calculation (mg/kg) = -[log10(sTfR x 1000/ferritin) -2.8229]/0.1207 from *Cogswell et al.*[22]

[d]Odds ratio of Control relative to BLISS

[e]Defined as body iron ≥0 mg/kg, haemoglobin ≥110 g/L and plasma ferritin ≥15 µg/L

[f]Defined as plasma ferritin <15 µg/L, in the absence of early functional iron deficiency and iron deficiency anaemia

[g]Defined as body iron <0 mg/kg and haemoglobin ≥110 g/L

[h]Defined as body iron <0 mg/kg and haemoglobin <110 g/L

For peer review only

Similar numbers had anaemia other than iron deficiency anaemia (13% BLISS, 10% Control; $p$=0.78).

Thirty-four participants had at least one biochemical value (not necessarily iron-related) outside the expected reference range for their age and were advised to contact their GP for follow up (n=19 Control, n=15 BLISS).

**Discussion**

We observed no significant differences in iron intake or status between infants following a baby-led approach to complementary feeding that had been modified to address concerns regarding iron intake, and infants following traditional spoon-feeding. However, iron intakes were low in both groups at 7 months (74% of infants at risk of inadequate intakes) and 17% had suboptimal iron status at 12 months.

Although many parents are choosing to follow BLW with their infant,[1-3] we know almost nothing about what these infants are eating, and how this might impact their health. Only one small observational study has evaluated intake in infants following unmodified BLW compared with age- and sex-matched infants following traditional spoon-feeding.[6] In that study, despite similar energy intakes, BLW infants had significantly lower intakes of iron than spoon-fed infants (1.6 mg/day vs 3.6 mg/day, $p$<0.001). By contrast, we found no difference in iron intakes in our study groups, and BLISS infants were consuming a median of 3.0 mg per day of iron, suggesting that encouraging the intake of 'high-iron' foods as part of a baby-led approach to complementary foods was effective in improving iron intakes.

For peer review only

Our BLISS intervention recommended that 'high-iron' foods, particularly red meat and iron-fortified infant cereal, should be offered at every meal, from the start of the complementary feeding period. Red meat is high in bioavailable haem iron,[27] and a higher intake has been associated with higher serum ferritin concentrations in toddlers,[28] and higher haemoglobin concentrations in very young children.[29] Similarly, iron-fortified infant cereal is high in iron and consumption has been shown to prevent iron deficiency anaemia.[30] In the current study, significantly more BLISS than Control infants were consuming red meat at 7 months. This was in contrast to an observational study suggesting that infants following unmodified BLW are no more likely to consume red meat than spoon-fed infants.[6] However, actual intakes were small in both groups, as they were for iron-fortified infant cereal. Other studies have also demonstrated relatively low intakes of both red meat[31] and iron fortified foods[32] in infants and toddlers. Therefore, further research is required to determine whether a more intensive intervention can feasibly increase the amount of these important iron sources consumed by both spoon-fed and baby-led infants.

Concern has been expressed regarding dietary exposure to inorganic arsenic through infant rice cereals and the potential health risks associated with high intakes in very young children.[33] Intakes of 3.0 µg/kg body weight per day have been estimated to increase the incidence of lung cancer by 0.5%,[34] but the European Food Safety Authority (EFSA) have estimated that a 6 month old infant would have to consume 90 g of rice based cereal per day in order to be exposed to a level of inorganic arsenic of approximately half that level (1.63 µg/kg body weight).[33] Given the maximum average intake in the current study was only 7.2 g per day of infant rice cereal, and the maximum observed intake was 75 g per day, it seems very unlikely that high intakes of inorganic arsenic are an issue in this population, even when consumption of iron fortified rice cereal is encouraged.

For peer review only

There was a high proportion (74% of both groups) of infants at risk of inadequate iron intakes at 7 months of age. Unfortunately, we do not have a measure of iron status at 7 months to determine whether this high prevalence of inadequate intake is reflected in poor iron status. However, at 12 months of age the risk of inadequate intakes had decreased (23% of Controls, 26% of BLISS). It is possible that this high prevalence at 7 months of age may be due to the cut offs available for determining the risk of inadequate iron intakes - currently, there is no specific cut off for infants less than 8 months of age that has the Institute of Medicine probabilities of inadequacy that are needed in order to calculate the prevalence of inadequacy.[35]

The BLISS study focused on iron deficiency anaemia, but 10% of Control infants and 13% of BLISS infants were diagnosed as having anaemia that was not concurrent with iron deficiency. Non-iron-deficient anaemia can be caused by a wide range of conditions, including infection (e.g., with malaria, HIV, or hookworm), folate or Vitamin B12 deficiency, or genetic disorders such as thalassemia and sickle cell anaemia.[36] We took care to minimise rates of infection in our study design, and malaria, HIV and hookworm are extremely rare in this age group in New Zealand. Similarly, no participant had a mean cell >86 fL which would be indicative of the megaloblastic anaemia of folate or Vitamin B12 deficiency.[37] We cannot rule out haemoglobinopathies as a cause of anaemia for some of the infants, but these would be fairly rare in this population. An alternative explanation for the high proportion of other anaemia could be the cut off used for defining anaemia (<110 g/L).[36,37] This value has been extrapolated from older age groups,[38] and there has been some discussion as to whether a lower cut off may be more appropriate in this age group.[39]

For peer review only

The current study suggests that when parents following a baby-led approach to complementary feeding are given advice to offer infants 'high-iron' foods with every meal, their iron status is similar to Control infants. This finding is important given health professionals' concerns that baby-led approaches to complementary feeding may increase the risk of iron deficiency,[3,4] and the observation that infants following unmodified BLW have significantly lower iron intakes.[6] Although we did not reach our planned sample size, it is important to note the most extreme difference in plasma ferritin concentration consistent with the data was -10.9 μg/L (i.e. the lower confidence limit for the difference). This suggests that, in response to a BLISS intervention, the Control group's median plasma ferritin concentration might, at most, fall to 18.0 μg/L – a value above the cutoffs usually associated with deficiency (i.e. 12 or 15 μg/L). The data are also consistent with plasma ferritin rising to 34.7 μg/L (applying the upper confidence limit). Similarly, the confidence limits for the differences in dietary iron intake at 7 and 12 months of age suggest that any differences may be too small to be of clinical interest with plausible ranges of -1 to 2.3 at 7 months and -1.6 to 1.4 at 12 months.

Our study has a number of strengths including being the first randomised controlled trial to investigate the impact of a baby-led approach to complementary feeding on iron intake and status. We collected robust dietary data using three non-consecutive days of weighed diet records. As infants often do not eat all of the food offered to them we asked parents to weigh the food before and after eating (including food that was no longer on the surface on which it was originally offered) to ensure we had as accurate a representation of actual consumption as was possible in a free-living population. The study had limited power to detect differences of 5.0 μg/L in geometric mean plasma ferritin concentrations because blood samples were obtained from 119 participants rather than the planned 168. However, the confidence intervals

For peer review only

enable the reader to see the range of plausible differences in plasma ferritin between the groups. Also, estimated breast milk volumes were used. This approach is commonly used when other methods are not feasible[32,40-44] but does mean that we do not have specific intake values for individuals. Finally, it was not considered ethical to randomise participants to follow an unmodified version of BLW because of concerns about its safety.[3,4] Therefore, the results should not be used to make conclusions about the iron status of infants following unmodified BLW.

**Conclusions**

There was no evidence of a difference in iron intakes and status between spoon-fed infants and infants following this modified version of BLW in which parents were given advice to offer 'high-iron' foods with each meal. This suggests that a baby-led approach can be used without impacting negatively on iron status. However, it is important to note that this study assessed a modified version of BLW so no conclusions can be made about the risk of iron deficiency in infants following unmodified BLW.

**Acknowledgments**

We would like to acknowledge all the families who participated in the BLISS study, as well as the research staff involved from the Departments of Human Nutrition and Medicine at the University of Otago.

For peer review only

## Figure legend

**Figure 1.** Flow of participants through the study

## Table legend

**Table 1.** Characteristics of participants who provided intake data at 7 and/or 12 months of age or biochemical data at 12 months of age

**Table 2.** Intake of iron and key absorption modifiers at 7 and 12 months of age from complementary foods and infant milks

**Table 3.** Iron from complementary foods at 7 and 12 months of age (consumers and non-consumers)

**Table 4.** Iron status indicators and categories at 12 months of age

For peer review only

## References

1 Cameron SL, Taylor RW, Heath A-LM. Parent-led or baby-led? Associations between complementary feeding practices and health-related behaviours in a survey of New Zealand families. *BMJ Open* 2013;3:1–9.

2 Brown, Lee. A descriptive study investigating the use and nature of baby-led weaning in a UK sample of mothers. *Maternal Child Nutr* 2011;7:34–47.

3 D'Andrea E, Jenkins K, Mathews M. Baby-led Weaning: A Preliminary Investigation. *Can J Diet Pract Res* 2016;77:1–6.

4 Cameron SL, Heath A-LM, Taylor RW. Healthcare professionals' and mothers' knowledge of, attitudes to and experiences with, Baby-Led Weaning: a content analysis study. *BMJ Open* 2012;2:1–9.

5 Rapley G, Murkett T. *Baby-led Weaning: Helping your Baby to Love Good Food*. London: Vermillon 2008.

6 Morison BJ, Taylor RW, Haszard JJ, *et al.* How different are baby-led weaning and conventional complementary feeding? A cross-sectional study of infants aged 6–8 months. *BMJ Open* 2016;6:1–11.

7 Domellöf M, Braegger C, Campoy C, *et al.* Iron requirements of infants and toddlers. *J Pediatr Gastroenterol Nutr* 2014;58:119–29.

8 Lozoff B, Beard J, Connor J, *et al.* Long-Lasting Neural and Behavioral Effects of Iron Deficiency in Infancy. *Nut Rev* 2006;64:34–43.

9 Congdon EL, Westerlund A, Algarin CR, *et al.* Iron Deficiency in Infancy is Associated with Altered Neural Correlates of Recognition Memory at 10 Years. *J Pediatr* 2012;160:1027–33.

10 Taylor RW, Williams SM, Fangupo LJ, *et al.* Effect of a Baby-Led Approach to Complementary Feeding on Infant Growth and Overweight. *JAMA Pediatr* 2017;171:838-846.

11 Fangupo LJ, Heath A-LM, Williams SM, *et al.* A Baby-Led Approach to Eating Solids and Risk of Choking. *Pediatrics* 2016;138:1–10.

12 Daniels L, Heath A-LM, Williams SM, *et al.* Baby-Led Introduction to SolidS (BLISS) study: a randomised controlled trial of a baby-led approach to complementary feeding. *BMC Pediatr* 2015;15:1–15.

13 Ministry of Health New Zealand. Well Child/Tamariki Ora services. Wellington: 2014 (accessed 30 July 2017). http://www.health.govt.nz/our-work/life-stages/child-health/well-child-tamariki-ora-services

14 Cameron SL, Taylor RW, Heath A-LM. Development and pilot testing of Baby-Led Introduction to SolidS - a version of Baby-Led Weaning modified to address concerns about iron deficiency, growth faltering and choking. *BMC Pediatr* 2015;15:1–11.

For peer review only

15 Ministry of Health New Zealand. New Zealand food composition database (FOODfiles). 2010 (accessed 4 July 2014). www.foodcomposition.co.nz/foodfiles.

16 Ministry of Health New Zealand, University of Otago New Zealand. Methodology report for the 2008/09 New Zealand adult nutrition survey. Wellington: Ministry of Health, 2011 (accessed 20 April 2017). http://www.health.govt.nz/publication/methodology-report-2008-09-nz-adult-nutrition-survey9-new-zealand-adult-nutrition-survey/oclc/756914555

17 Clousten A. *The role of commercial processed baby foods in the diets of New Zealand toddlers*. Thesis, Master of Dietetics. University of Otago, New Zealand. 2014. http://hdl.handle.net/10523/5492.

18 Dewey KG, Heinig MJ, Nommsen LA, *et al.* Adequacy of energy intake among breast-fed infants in the DARLING study: relationships to growth velocity, morbidity, and activity levels. *J Pediatr* 1991;119:538–47.

19 Barris A. *Meat and haem iron intakes of New Zealand toddlers aged 12-24 months*. Thesis, Master of Dietetics. University of Otago, New Zealand. 2012. http://hdl.handle.net/10523/3839.

20 Hartley N. *Phytate and zinc intakes of toddlers from New Zealand*. Thesis, Master of Dietetics. University of Otago, New Zealand. 2013. http://hdl.handle.net/10523/4645.

21 Thurnham DI, McCabe LD, Haldar S, *et al.* Adjusting plasma ferritin concentrations to remove the effects of subclinical inflammation in the assessment of iron deficiency: a meta-analysis. *Am J Clin Nutr* 2010;92:546–55.

22 Cogswell ME, Looker AC, Pfeiffer CM, *et al.* Assessment of iron deficiency in US preschool children and nonpregnant females of childbearing age: National health and nutrition examination survey 2003-2006. *Am J Clin Nutr* 2009;89:1334–42.

23 Harttig U, Haubrock J, Knüppel S, *et al.* The MSM program: web-based statistics package for estimating usual dietary intake using the Multiple Source Method. *Eur J Clin Nutr* 2011;65:S87–S91.

24 Gibson RS, Ferguson EL. An interactive 24-hour recall for assessing the adequacy of iron and zinc intakes in developing countries. *HarvestPlus Technical Monograph* 2008:1–160.

25 Atkinson J, Salmond C, Crampton P. *NZDep2013 Index of Deprivation User's Manual*. Department of Public Health, University of Otago, Wellington and Division of Health Sciences, University of Otago, New Zealand 2014.

26 European Food Safety Authority (EFSA) Panel on Dietetic Products Nutrition and Allergies. Scientific Opinion on Dietary Reference Values for Iron. 2015:1–115.

For peer review only

27 Lombardi-Boccia G, Dominguez BM, Aguzzi A. Total heme and non-heme iron in raw and cooked meats. *Food Chem Toxicol* 2002;**67**:1–4.

28 Szymlek-Gay EA, Ferguson EL, Heath A-LM, *et al.* Food-based strategies improve iron status in toddlers: a randomized controlled trial. *Am J Clin Nutr* 2009;**90**:1541–51.

29 Olaya GA, Lawson M, Fewtrell MS. Efficacy and safety of new complementary feeding guidelines with an emphasis on red meat consumption: a randomized trial in Bogota, Colombia. *Am J Clin Nutr* 2013;**98**:983–93.

30 Walter T, Dallman PR, Pizarro F, *et al.* Effectiveness of iron-fortified infant cereal in prevention of iron-deficiency anemia. *Pediatrics* 1993;**91**:976–82.

31 Fox MK, Reidy K, Novak T, *et al.* Sources of Energy and Nutrients in the Diets of Infants and Toddlers. *J Am Diet Assoc* 2006;**106**:S28–S42.

32 Wall CR, Brunt DR, Grant CC. Ethnic variance in iron status: is it related to dietary intake? *PHN* 2008;**12**:1413–21.

33 European Food Safety Authority (EFSA) Panel on Contaminants in the Food Chain (CONTAM). Scientific Opinion on Arsenic in Food. *EFSA Journal* 2009;**7**:1351–199.

34 World Health Organization. Joint FAO/WHO Expert Committee On Food Additives: Summary and Conclusions. 2010:1–16.

35 Institute of Medicine, Food and Nutrition Board. *Dietary reference intakes: vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc*. Washington, DC: National Academy Press 2001.

36 World Health Organization. *Iron deficiency anaemia: assessment, prevention and control: a guide for programme managers*. Geneva: World Health Organization 2001.

37 Southern Community Laboratories Ltd. Southern Community Laboratories Paediatric Reference Ranges. Southern Community Laboratories 2014.

38 Gibson RS. *Principles of Nutritional Assessment: Chapter 17 Assessment of iron status*. 2nd ed. New York: Oxford University Press 2005.

39 Domellöf M, Dewey KG, Lönnerdal B, *et al.* The diagnostic criteria for iron deficiency in infants should be reevaluated. *J Nutr* 2002;**132**:3680–6.

40 Skinner JD, Carruth BR, Houck KS, *et al.* Longitudinal Study of Nutrient and Food Intakes of Infants Aged 2 to 24 Months. *J Am Diet Assoc* 1997;**97**:496–504.

41 Devaney B, Ziegler P, Pac S, *et al.* Nutrient intakes of infants and toddlers. *J Am Diet Assoc* 2004;**104**:S14–S21.

42 Ponza M, Devaney B, Ziegler P, *et al.* Nutrient intakes and food choices of

For peer review only

infants and toddlers participating in WIC. *J Am Diet Assoc* 2004;**104**:S71–9.

43 Briefel RR, Kalb LM, Condon E, *et al.* The Feeding Infants and Toddlers Study 2008: Study Design and Methods. *J Am Diet Assoc* 2010;**110**:S16–S26.

44 Sharma S, Kolahdooz F, Butler L, *et al.* Assessing dietary intake among infants and toddlers 0–24 months of age in Baltimore, Maryland, USA. *Nutr J* 2013;**12**:1–7.

For peer review only

**Contributorship Statement:**

A-LMH and RWT conceived and designed the research. LD contributed to the design of the iron-related components of the research, collected data, and prepared the first full and subsequent drafts of this manuscript. SMW and JJH advised on study design and performed statistical analyses. RSG, EAF, BJW and BJT provided expert input into the design of the study and ongoing advice and support. All authors made an important intellectual contribution to this manuscript, and approved the final manuscript as submitted.

For peer review only

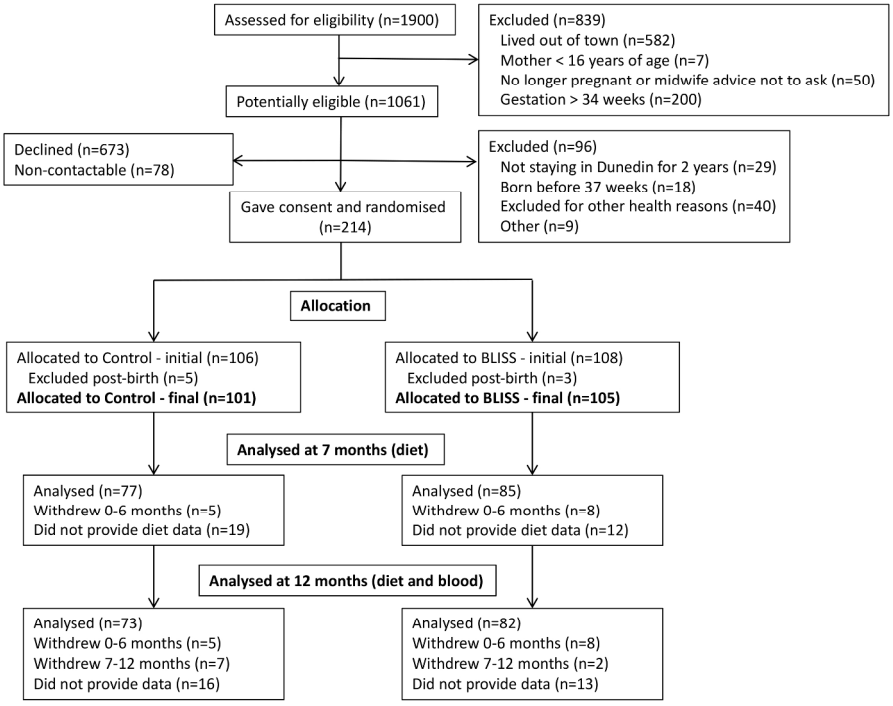



Figure 1. Flow of participants through the study

254x190mm (300 x 300 DPI)

For peer review only

## Supplemental Tables

**eTable 1** Comparison of characteristics of participants who provided either intake or status data so were included in this analysis, and whose who provided neither intake nor status data so were not included.

**eTable 2** Milk consumers at 7 and 12 months of age

**eTable 3** Number of consumers of each food group at 7 months of age

**eTable 4** Dietary sources of iron for consumers only at 7 months of age (complementary foods and infant milks)

**eTable 5** Number of consumers of each food group at 12 months of age

**eTable 6** Dietary sources of iron for consumers only at 12 months of age (complementary foods and infant milks)

For peer review only

**eTable 1** Comparison of characteristics of participants included (provided either intake or status data) and not included (provided neither intake nor status data)[a]

| | Included (*n*=169) | Not included (*n*=37) | *p* |
|---|---|---|---|
| **Maternal and household variables** | | | |
| Maternal age at birth (years), mean (SD) | 31.9 (5.3) | 28.3 (5.8) | **<0.001** |
| Maternal parity | | | 0.79 |
| First child | 69 (41) | 16 (43) | |
| Two children | 64 (38) | 11 (30) | |
| 3 or more children | 36 (21) | 10 (27) | |
| Maternal ethnicity | | | 0.45 |
| NZ European | 141 (83) | 27 (73) | |
| Māori | 14 (8.5) | 6 (16) | |
| Other | 14 (8.5) | 4 (11) | |
| Maternal education | | | 0.29 |
| School only | 49 (29) | 14 (38) | |
| Post-secondary | 33 (20) | 10 (27) | |
| University | 87 (51) | 13 (35) | |
| Household deprivation[b] | | | 0.92 |
| 1-3 (Low) | 49 (29) | 11 (30) | |
| 4-7 | 83 (49) | 19 (51) | |
| 8-10 (High) | 37 (22) | 7 (19) | |

For peer review only

| | Included (*n*=169) | Not included (*n*=37) | *p* |
|---|---|---|---|
| **Infant variables** | | | |
| Sex | | | 0.29 |
| Female | 87 (51) | 22 (61) | |
| Male | 82 (49) | 14 (39) | |
| Infant birth weight (g), mean (SD) | 3503 (449) | 3619 (545) | 0.18 |
| Infant gestational age at birth (weeks), mean (SD) | 39.6 (1.1) | 39.6 (1.0) | 0.95 |

Abbreviations: NZ European, New Zealand European

**Bold** indicates a statistically significant difference at $p<0.05$

[a]Data presented as *n* (%), unless otherwise stated

[b]Household deprivation categorised using the NZDep2013 scale in which decile 1 indicates the lowest level of deprivation and 10 indicates the highest[25]

For peer review only

**eTable 2** Milk consumers at 7 and 12 months of age[a,b]

| | Total | Control | BLISS | *p* Value |
|---|---|---|---|---|
| **7 months of age** | n=162 | n=77 | n=85 | |
| Breast milk only | 82 (51) | 38 (49) | 44 (52) | 0.95 |
| Infant formula only | 39 (24) | 19 (25) | 20 (23) | |
| Mixed (breast milk and infant formula) | 41 (25) | 20 (26) | 21 (25) | |
| **12 months of age** | n=143 | n=68 | n=75 | |
| Breast milk only | 62 (43) | 31 (46) | 31 (41) | 0.94 |
| Infant formula only | 47 (33) | 22 (32) | 25 (33) | |
| Mixed (breast milk and infant formula) | 15 (11) | 7 (10) | 8 (11) | |
| None of the above | 19 (13) | 8 (12) | 11 (15) | |
| Cow's milk[c] | | | | |
| None | 92 (64) | 47 (69) | 45 (60) | 0.51 |
| < 500mL/day | 40 (28) | 17 (25) | 23 (31) | |
| ≥ 500mL/day | 11 (8) | 4 (6) | 7 (9) | |

[a]Data presented as n (%)
[b]Based on intake reported during the three-day weighed diet records, collected at 7 and 12 months of age
[c]Cow's milk consumed as a drink

For peer review only

**eTable 3** Number of consumers of each food group at 7 months of age[a,b,c]

| | Control | BLISS | *p* Value |
|---|---|---|---|
| Breads and cereals[d] | 77 (100) | 85 (100) | - |
| Miscellaneous[e] | 77 (100) | 85 (100) | - |
| Vegetables | 75 (97) | 84 (99) | 0.50 |
| Fruit and fruit juice | 73 (95) | 81 (95) | 0.89 |
| Dairy | 66 (86) | 82 (96) | **0.015** |
| Breast milk | 58 (75) | 65 (76) | 0.87 |
| Red meat[f] | 42 (55) | 65 (76) | **0.003** |
| Iron-fortified infant cereal | 39 (51) | 62 (73) | **0.003** |
| Infant formula | 39 (51) | 41 (48) | 0.76 |
| Other meat[g] | 38 (49) | 45 (53) | 0.65 |
| Legumes, nuts, seeds and eggs | 26 (34) | 71 (84) | **<0.001** |

[a]Data presented as n (%)
[b]Intake reported during the three-day weighed diet records collected at 7 months of age
[c]Ordered by number of consumers in the Control group from highest to lowest
[d]Breads and cereals other than iron-fortified infant cereals
[e]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.
[f]Red meat defined as: beef, lamb, mutton, venison
[g]Other meat defined as: fish, poultry, pork, processed meats

For peer review only

**eTable 4** Dietary sources of iron for consumers only[a] at 7 months of age (complementary foods and infant milks)[b,c,d]

| | Control | | BLISS | | Difference (95% CI)[e] | *p* Value |
|---|---|---|---|---|---|---|
| | g/day | mg/day | g/day | mg/day | | |
| Infant formula | 309 (110, 745) | 5.5 (1.2, 8.3) | 525 (136, 804) | 6.0 (2.7, 7.5) | 0.5 (-2.0, 3.0) | 0.70 |
| Iron-fortified infant cereal | 4.0 (2, 9) | 0.72 (0.3, 1.3) | 1.7 (0.5, 5) | 0.37 (0.1, 0.9) | -0.3 (-0.7, -0.0) | **0.041** |
| Breast milk | 750 (660, 750) | 0.52 (0.46, 0.53) | 750 (660, 750) | 0.52 (0.48, 0.53) | 0.0 (-0.0, 0.0) | 0.99 |
| Vegetables | 34.8 (12, 72) | 0.16 (0.1, 0.4) | 20.5 (10, 43) | 0.10 (0.0, 0.2) | -0.06 (-0.1, 0.0) | 0.06 |
| Fruit and fruit juice | 55.6 (19, 94) | 0.14 (0.1, 0.3) | 39.5 (16, 69) | 0.10 (0.0, 0.2) | -0.0 (-0.1, 0.0) | 0.21 |
| Red meat[f] | 3.8 (1, 9) | 0.13 (0.0, 0.4) | 3.2 (1, 6) | 0.11 (0.0, 0.2) | -0.0 (-0.1, 0.1) | 0.50 |
| Breads and cereals[g] | 7.8 (2, 18) | 0.11 (0.0, 0.3) | 15.5 (8, 28) | 0.26 (0.1, 0.4) | 0.15 (0.1, 0.2) | **<0.001** |
| Legumes, nuts, seeds and eggs | 3.7 (1, 7) | 0.06 (0.01, 0.2) | 3.1 (1, 9) | 0.05 (0.0, 0.2) | -0.0 (-0.1, 0.0) | 0.41 |
| Other meat[h] | 3.6 (2, 8) | 0.04 (0.01, 0.1) | 4.7 (2, 9) | 0.04 (0.02, 0.1) | 0.0 (-0.0, 0.0) | 0.90 |
| Miscellaneous[i] | 40.0 (10, 85) | 0.01 (0.0, 0.1) | 32.8 (10, 61) | 0.02 (0.0, 0.1) | -0.0 (-0.0, 0.0) | 0.99 |
| Dairy | 10.8 (0.4, 29) | 0.0 (0.0, 0.0) | 9.4 (2, 24) | 0.0 (0.0, 0.0) | 0.0 (-0.0, 0.0) | 0.27 |

[a]Refer to eTable 3 for the number of consumers of each food group at 7 months of age
[b]Data presented as median (25$^{th}$, 75$^{th}$ percentile)
[c]Intake reported during the three-day weighed diet records collected at 7 months of age
[d]Ordered from highest to lowest food group contributing to total iron intakes in the Control group
[e]Difference in median iron (mg/day) intake between groups: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control
[f]Red meat defined as: beef, lamb, mutton, venison
[g]Breads and cereals other than iron-fortified infant cereals
[h]Other meat defined as: fish, poultry, pork and processed meats
[i]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.

For peer review only

**eTable 5** Number of consumers of each food group at 12 months of age[a,b,c]

| | Control | BLISS | *p* Value |
|---|---|---|---|
| Breads and cereals[d] | 68 (100) | 75 (100) | - |
| Miscellaneous[e] | 68 (100) | 75 (100) | - |
| Dairy | 68 (100) | 74 (99) | 0.34 |
| Vegetables | 67 (99) | 75 (100) | 0.29 |
| Fruit and fruit juice | 66 (97) | 72 (96) | 0.73 |
| Other meat[f] | 57 (84) | 67 (89) | 0.33 |
| Legumes, nuts, seeds and eggs | 55 (81) | 66 (88) | 0.24 |
| Red meat[g] | 41 (60) | 53 (71) | 0.19 |
| Breast milk | 38 (56) | 39 (52) | 0.64 |
| Infant formula | 29 (43) | 33 (44) | 0.87 |
| Iron-fortified infant cereal | 14 (21) | 21 (28) | 0.30 |

[a]Data presented as n (%)
[b]Intake reported during the three-day weighed diet records collected at 12 months of age
[c]Ordered by number of consumers in the Control group from highest to lowest
[d]Breads and cereals other than iron-fortified infant cereals
[e]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.
[f]Other meat defined as: fish, poultry, pork, processed meats
[g]Red meat defined as: beef, lamb, mutton, venison

For peer review only

**eTable 6** Dietary sources of iron for consumers only[a] at 12 months of age (complementary foods and infant milks)[b,c,d]

| | Control | | BLISS | | Difference (95% CI)[e] | *p* Value |
|---|---|---|---|---|---|---|
| | g/day | mg/day | g/day | mg/day | | |
| Infant formula | 414 (274, 569) | 4.9 (3.5, 6.4) | 329 (87, 524) | 3.8 (1.5, 5.4) | -1.1 (-2.9, 0.7) | 0.23 |
| Iron-fortified infant cereal | 7.2 (3, 15) | 1.2 (0.6, 3.5) | 3.3 (2, 5) | 0.73 (0.4, 1.2) | -0.7 (-1.8, 0.4) | 0.22 |
| Breads and cereals[f] | 57.1 (39, 74) | 0.84 (0.5, 1.6) | 60.2 (47, 82) | 1.10 (0.6, 1.8) | 0.2 (-0.2, 0.5) | 0.26 |
| Vegetables | 64.6 (45, 97) | 0.39 (0.2, 0.5) | 55.5 (26, 73) | 0.29 (0.1, 0.5) | -0.1 (-0.2, -0.0) | **0.023** |
| Miscellaneous[g] | 132 (89, 205) | 0.32 (0.1, 0.6) | 119 (67, 235) | 0.18 (0.1, 0.5) | -0.1 (-0.3, 0.0) | 0.05 |
| Breast milk | 448 (448, 448) | 0.31 (0.3, 0.31) | 448 (443, 448) | 0.31 (0.3, 0.31) | -0.0 (-0.0, 0.0) | 0.54 |
| Fruit and fruit juice | 94.4 (52, 132) | 0.27 (0.2, 0.5) | 106 (60, 165) | 0.32 (0.2, 0.5) | 0.1 (-0.0, 0.2) | 0.31 |
| Red meat[h] | 9.2 (5, 19) | 0.27 (0.1, 0.6) | 9.4 (4, 15) | 0.28 (0.1, 0.5) | 0.0 (-0.2, 0.2) | 0.89 |
| Other meal[i] | 17.7 (8, 28) | 0.21 (0.1, 0.3) | 15.7 (8, 27) | 0.19 (0.1, 0.3) | -0.0 (-0.1, 0.1) | 0.64 |
| Legumes, nuts, seeds and eggs | 7.2 (3, 25) | 0.14 (0.0, 0.4) | 11.2 (5, 23) | 0.20 (0.1, 0.4) | 0.1 (-0.0, 0.2) | 0.27 |
| Dairy | 84.4 (34, 188) | 0.06 (0.0, 0.1) | 109 (51, 188) | 0.06 (0.0, 0.1) | 0.0 (-0.0, 0.0) | 0.82 |

[a]Refer to eTable 5 for the number of consumers of each food group at 12 months of age
[b]Data presented as median (25$^{th}$, 75$^{th}$ percentile)
[c]Intake reported during the three-day weighed diet records collected at 12 months of age
[d]Ordered from highest to lowest food group contributing to total iron intakes in the Control group
[e]Difference in median iron (mg/day) intake between groups: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control
[f]Breads and cereals other than iron-fortified infant cereals
[g]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.
[h]Red meat defined as: beef, lamb, mutton, venison
[i]Other meat defined as: fish, poultry, pork, processed meats

For peer review only

## Checklist of items to include when reporting a randomized trial (56-58)

| PAPER SECTION<br>And topic | Item | Description | Reported on page # |
|---|---|---|---|
| *TITLE & ABSTRACT* | 1 | How participants were allocated to interventions (*e.g.*, "random allocation", "randomized", or "randomly assigned"). | 1, 5 |
| *INTRODUCTION*<br>Background | 2 | Scientific background and explanation of rationale. | 7 |
| *METHODS*<br>Participants | 3 | Eligibility criteria for participants and the settings and locations where the data were collected. | 8 |
| Interventions | 4 | Precise details of the interventions intended for each group and how and when they were actually administered. | 8-9 |
| Objectives | 5 | Specific objectives and hypotheses. | 7 |
| Outcomes | 6 | Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors). | 7 |
| Sample size | 7 | How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules. | 12 |
| Randomization --<br>Sequence generation | 8 | Method used to generate the random allocation sequence, including details of any restriction (*e.g.*, blocking, stratification). | 8 |
| Randomization --<br>Allocation concealment | 9 | Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned. | 8 |
| Randomization --<br>Implementation | 10 | Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups. | 8 |
| Blinding (masking) | 11 | Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. When relevant, how the success of blinding was evaluated. | 10 |
| Statistical methods | 12 | Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses. | 12-13 |
| RESULTS<br><br>Participant flow | 13 | Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons. | Figure 1 |
| Recruitment | 14 | Dates defining the periods of recruitment and follow-up. | 8, Figure 1 |
| Baseline data | 15 | Baseline demographic and clinical characteristics of each group. | Table 1 |
| Numbers analyzed | 16 | Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat" . State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%). | 12, tables |
| Outcomes and estimation | 17 | For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval). | 13-15 |
| Ancillary analyses | 18 | Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory. | 13-15 |
| Adverse events | 19 | All important adverse events or side effects in each intervention group. | 12 |
| DISCUSSION<br>Interpretation | 20 | Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes. | 15-18 |
| Generalizability | 21 | Generalizability (external validity) of the trial findings. | 15-18 |
| Overall evidence | 22 | General interpretation of the results in the context of current evidence. | 15-18 |

For peer review only

BMJ Open

# Impact of a modified version of Baby-Led Weaning on iron intake and status: a randomised controlled trial

| | |
|---|---|
| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2017-019036.R2 |
| Article Type: | Research |
| Date Submitted by the Author: | 09-Mar-2018 |
| Complete List of Authors: | Daniels, Lisa; University of Otago, Human Nutrition; University of Otago, Medicine<br>Taylor, Rachael; University of Otago, Medicine<br>Williams, Sheila; University of Otago, Preventive and Social Medicine<br>Gibson, R; University of Otago, Human Nutrition<br>Fleming, Elizabeth; University of Otago, Human Nutrition; University of Otago, Medicine<br>Wheeler, Benjamin; University of Otago, Women's and Children's Health<br>Taylor, Barry; University of Otago, Women's and Children's Health<br>Haszard, Jillian; University of Otago, Human Nutrition<br>Heath, Anne-Louise; University of Otago, Human Nutrition |
| Primary Subject Heading: | Nutrition and metabolism |
| Secondary Subject Heading: | Paediatrics, Public health |
| Keywords: | Baby-led weaning, Complementary feeding, Dietary iron, Iron status, Iron deficiency, Infants |
| | |

SCHOLARONE™
Manuscripts

# Impact of a modified version of Baby-Led Weaning on iron intake and status: a randomised controlled trial

Lisa Daniels, PhD[1,2]

Rachael W Taylor, PhD[2]

Sheila M Williams, DSc[3]

Rosalind S Gibson, PhD[1]

Elizabeth A Fleming, MCapSci[1,2]

Benjamin J Wheeler, FRACP[4]

Barry J Taylor, FRACP[4]

Jillian J Haszard, PhD[1]

*Anne-Louise M Heath, PhD[1]

[1]Department of Human Nutrition, University of Otago, PO Box 56, Dunedin 9054, New Zealand

[2]Department of Medicine, University of Otago, PO Box 56, Dunedin 9054, New Zealand

[3]Department of Preventive and Social Medicine, University of Otago, PO Box 56, Dunedin 9054, New Zealand

[4]Department of Women's and Children's Health, University of Otago, PO Box 56, Dunedin 9054, New Zealand

*** Corresponding author**

Anne-Louise M Heath

Department of Human Nutrition

For peer review only

University of Otago

PO Box 56

Dunedin 9054

New Zealand

Telephone: +64 3 479 8379

Email: anne-louise.heath@otago.ac.nz

**Funding statement:** This work was supported by Meat & Livestock Australia, Lottery Health Research, Karitane Products Society, Perpetual Trustees, the University of Otago, and the New Zealand Federation of Women's Institutes. The funders provided funds only and played no role in the study design, development of the study aims, carrying out the study or the analysis, or interpretation of the results. Heinz Wattie's Limited provided baby rice cereal for participants in the intervention group. Part of Professor R Taylor's salary is from a Karitane Products Society (KPS) Fellowship that is paid via the University of Otago. Dr L Daniels was supported by a University of Otago Doctoral Scholarship, and a University of Otago Postgraduate Publishing Bursary.

**Competing interests statement:** We have read and understood the BMJ policy on declaration of interests and declare that we have no competing interests.

**Clinical Trial Registration:** Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au). Identifier ACTRN12612001133820.

**Data Sharing Statement:** No additional data are available.

**Abbreviations**

For peer review only

| | |
|---|---|
| AGP | $\alpha_1$-acid glycoprotein |
| BLW | Baby-Led Weaning |
| BLISS | Baby-Led Introduction to SolidS |
| CRP | C-reactive protein |
| EFSA | European Food Safety Authority |
| GP | general practitioner |
| MFP | 'meat, fish, poultry' |
| sTfR | soluble transferrin receptor |
| WDR | weighed three-day diet record |

**Abstract word count:** 282

**Word count:** 4,236

For peer review only

**Abstract**

**Objective:** To determine the iron intake and status of infants following a version of Baby-Led Weaning (BLW) modified to prevent iron deficiency (Baby-Led Introduction to SolidS; BLISS) compared to those of infants following traditional spoon-feeding.

**Design, participants and intervention:** This randomised controlled trial included 206 participants assigned to Control (n=101) or BLISS (n=105) groups. Both groups received standard midwifery and 'Well Child' care. BLISS participants received eight additional visits (from before birth to 9 months) providing education and support on the BLISS approach to complementary feeding (i.e. BLW modified to increase iron intake). The primary outcome of the BLISS study (growth) has been previously reported. This paper reports the key pre-specified secondary outcomes iron intake and iron status.

**Outcome measures:** Intake of iron and key absorption modifiers was assessed using weighed three-day diet records at 7 and 12 months. A venipuncture blood sample was collected at 12 months to determine plasma ferritin, haemoglobin, soluble transferrin receptor, C-reactive protein, and $\alpha_1$-acid glycoprotein concentrations; and body iron was calculated.

**Results:** Differences in median dietary iron intakes between the Control and BLISS groups were not significant at 7 (difference 0.6 mg/day; 95% CI: -1.0 to 2.3) or 12 (-0.1 mg/day; -1.6 to 1.4) months of age. Similarly, there were no significant differences in plasma ferritin concentration (difference -2.6 µg/L; 95% CI: -10.9 to 5.8), body iron (0.04 mg/kg; -1.1 to 1.2), or the prevalence of depleted iron stores, early functional iron deficiency, or iron deficiency anaemia (all $p \geq 0.65$) at 12 months of age.

**Conclusions:** A baby-led approach to complementary feeding does not appear to increase the risk of iron deficiency in infants when their parents are given advice to offer 'high-iron' foods with each meal.

For peer review only

**Trial registration:** Australian New Zealand Clinical Trials Registry (http://www.anzctr.org.au). Identifier ACTRN12612001133820.

**Keywords:** Baby-led weaning, complementary feeding, dietary iron, iron status, iron deficiency, body iron, infants, toddlers

For peer review only

## Article summary

### Strengths and limitations of this study:

- First randomised controlled trial to investigate the impact of a baby-led approach to complementary feeding on iron intake and biochemical iron status.
- Robust dietary assessment data provided by weighed diet records collected on non-consecutive days.
- Did not reach planned sample size, but confidence intervals are provided to indicate the range of plausible values in the population.
- This trial cannot be used to draw conclusions about the risk of iron deficiency in infants following unmodified BLW.

For peer review only

## Introduction

Anecdotal reports suggest that many parents are following Baby-Led Weaning (BLW) with their infants, particularly in New Zealand,[1] the United Kingdom,[2] and Canada.[3] However, health professionals have expressed concerns about this alternative approach to complementary feeding that need to be addressed.[3,4] Infants following BLW are expected to feed themselves *all* of their food from the start of the complementary feeding period[5] and it has been proposed that this may increase the risk of iron deficiency if the majority of first foods offered are foods low in iron, such as fruits and vegetables, or if iron-fortified infant cereals are avoided due to their semi-liquid consistency.[6] A recent observational study reported that mean dietary iron intake in infants following BLW was less than half that of infants following traditional spoon-feeding.[6] However, the impact of this lower iron intake on the biochemical iron status of infants has not been examined in that[6] or any other study.

Iron deficiency that progresses to iron deficiency anaemia can impact on the central nervous system and development during infancy, leading to poorer cognitive and behavioural performance.[7] Moreover, these impacts on infant development may not be reversible.[8,9] It is important, therefore, to determine whether a baby-led approach can be followed without increasing the risk of iron deficiency before baby-led approaches can be considered an appropriate alternative to traditional complementary feeding practices.

The aim of the Baby-led Introduction to SolidS (BLISS) study was to determine whether a modified version of BLW prevents young children from becoming overweight,[10] without increasing their risk of iron deficiency, growth faltering,[10] and choking.[11] In this paper we report the key pre-specified secondary outcomes iron intake (at 7 and 12 months of age)

For peer review only

and iron status (at 12 months) of infants following BLISS compared with traditional spoon-feeding.

**Methods**

Detailed methods have been described elsewhere[12] so only relevant information is included here. The Lower South Regional Ethics Committee (LRS/11/09/037) approved the study and adult participants gave written informed consent. Pregnant women in their third trimester of pregnancy who were booked into the Queen Mary Maternity Hospital in Dunedin, New Zealand were invited into the study between November 2012 and March 2014. Delayed cord clamping was infrequently practiced in Queen Mary Maternity Hospital at the time of the study. Women were eligible if they: spoke English or Te Reo Māori (the indigenous language of New Zealand); planned to live in Dunedin, New Zealand, until their child was at least 2 years of age; and were 16 years of age or older. Women were excluded if their infant was born before 37 weeks gestation, or had a congenital abnormality, physical condition or intellectual disability that was likely to affect their feeding or growth. Participants were randomised using random length blocks after stratification for parity (first child, subsequent child) and maternal education (tertiary, non-tertiary), to Control (n=101) or BLISS (n=105) groups by the study biostatistician. The BLISS study, and intervention, are not in any way related to the UK-based Bliss charity for "babies born premature or sick" (www.bliss.org.uk).

**Intervention**

The Control group participants received routine midwifery (until 6 weeks of age) and 'Well Child' care (from 6 weeks). 'Well Child Tamariki Ora' is a nationally funded program to support and educate families with children under 5 years of age. The program recommends

For peer review only

exclusive breastfeeding until around 6 months of age with the introduction of complementary foods at around 6 months.[13]

Participants in the BLISS group received routine midwifery and 'Well Child' care, and BLISS support and education from before birth (approximately 34-35 weeks gestation) until 9 months of age. The BLISS approach was based on three key principles of BLW: exclusive milk feeding until 6 months of age, infant self-feeding from the start of complementary feeding (i.e. baby-led from 6 months of age), and offering family foods as finger foods so they can be picked up by the infant. However, BLISS also included modifications to address the three main concerns about BLW expressed by health professionals:[3,4] iron deficiency, growth faltering,[10] and choking.[11]

The BLISS intervention comprised: 1) five contacts with a lactation consultant (from the third trimester of pregnancy to 6 months of age) to encourage and support exclusive milk feeding (ideally breastfeeding) and delay the introduction of complementary foods until 6 months of age, 2) three contacts with BLISS research staff to give individualised advice on how to follow BLISS (at 5.5, 7 and 9 months of age), and 3) a range of written resources that were developed to help parents follow BLISS,[14] including recipe books given at 5.5, 7 and 9 months of age, and lists of age-appropriate foods.[12] Parents were encouraged to offer their child three types of finger foods at every meal: a 'high-iron' food (e.g., red meat, iron-fortified infant cereal (in a hand held way, e.g., on toast)), an energy rich food (>1.5 kcal/g, e.g., avocado, cheese), and an easy to eat food such as fruit or vegetables. BLISS participants were provided with complementary packets of iron-fortified infant cereal (For Baby Rice Cereal, Heinz Watties Ltd., Australia) at each of the intervention visits (5.5, 7, and 9 months).

For peer review only

The iron content of this infant cereal was 2.2 mg per 100 g of infant cereal prepared with water.

**Adherence**

Questionnaires were used to determine adherence to BLISS by asking parents 'how has your baby been fed solids in the past week?' when their infant was 7 and 12 months of age. Adherence to BLISS was defined as the infant feeding themselves most or all of their food in the past week.

**Outcome Assessment**

Demographic data were collected at baseline by questionnaire, except for birth weight and gestational age which were obtained from hospital records. Research staff conducting measurement visits and administering questionnaires were blinded to group allocation. At 2, 4, 6, 7, 8, 9 and 12 months of age brief feeding questionnaires were used to collect information including the age when breastfeeding stopped and/or formula feeding started and stopped.

***Dietary Assessment***

Weighed three-day diet records (WDRs) were used to assess dietary intake at 7 and 12 months of age. Parent participants were given detailed instructions and provided with dietary scales (Salter Electronic, Salter Housewares Ltd. Tonbridge, UK) accurate to ±1 g. They then recorded everything their child ate and drank over three randomly assigned non-consecutive days (two week days and one weekend day) over a three week period. Parents were asked to record the total weight of food offered, and to collect, weigh and record all leftover food including food on the floor, baby, or the tray, so that the amount of food consumed by the infant could be calculated. Any supplements consumed were also recorded.

For peer review only

The WDRs were entered into Kai-culator (Version 1.13s, University of Otago, New Zealand), a dietary analysis program that includes dietary data from the New Zealand Food Composition Database (FOODfiles 2010, Plant and Food Research),[15] commonly consumed recipes from the 2008/09 New Zealand Adult Nutrition Survey,[16] and commercial infant foods collated by the research team.[17] It was not possible to directly measure breast milk intake so it was assumed to be 750 g per day at 7 months and 448 g per day at 12 months based on a quadratic curve fitted to the breast milk volumes reported by Dewey et al.[18] If the infant was fed both breast milk and infant formula then the gram amount of infant formula consumed was subtracted from the estimated total breast milk intake (i.e. 750 or 448 g per day).The iron content of breast milk was assumed to be 0.07 mg per 100 g.[15]

Grams of red meat, grams of 'meat, fish, poultry' (MFP), milligrams of haem iron,[19] and milligrams of phytate[20] were determined using values from the literature and information from manufacturers.

***Biochemical Assessment***

A non-fasting venous blood sample was obtained from 119 infants at 12 months of age (58% of total study participants). Of those who did not provide a blood sample, 26 blood draws were unsuccessful, 22 had withdrawn from the study by 12 months of age, 13 could not be contacted or were living out of town, and 26 parents did not provide consent for the blood test. Blood samples were drawn from an antecubital vein into a trace element-free lithium heparin anticoagulated tube (7.5 mL; S-Monovette, Sarstedt, Nümbrecht, Germany) and refrigerated immediately after collection. If the child was unwell the blood test was delayed

For peer review only

for 14 days.

Complete blood count (Sysmex XE 5000, Kobe, Japan) and plasma ferritin (Cobas 8000 unit e 602, Roche, USA) were determined on collection day by Southern Community Laboratories Ltd., (Dunedin, New Zealand). Aliquots of plasma were stored at -80°C until subsequent analysis of soluble transferrin receptor (sTfR), C-reactive protein (CRP), and $\alpha_1$-acid glycoprotein (AGP), using a Cobas C311 (Roche, USA) at the Department of Human Nutrition laboratories (University of Otago, Dunedin, New Zealand). Cutoffs of > 5 mg/L CRP and > 1 g/L AGP defined the presence of inflammation, for example as a result of infection. Ferritin multipliers were used to adjust ferritin concentrations to remove the influence of this inflammation.[21] The sTfR values were converted to be equivalent with the Flowers assay:[22] 1.5 x Roche sTfR + 0.35 mg/L and body iron (mg/kg) was calculated:[22] -[log10(sTfR x 1000/ferritin) -2.8229]/0.1207.

**Adverse Events**

Participants with biochemical results outside pre-defined clinical reference ranges for Complete Blood Count indices or plasma ferritin were contacted, informed of the abnormal result, and advised to visit their general practitioner for advice.

**Statistical Analysis**

The data were analysed according to modified intention to treat. A sample size of 84 participants per group provided 80% power ($\alpha$=0.05) to detect a difference in geometric mean plasma ferritin concentrations of 5.0 µg/L.[12]

For peer review only

The proportions of infants at 7 and 12 months of age fed breast milk, infant formula, or both ('mixed fed'), as well as those consuming cow's milk were determined using Chi-squared tests. All nutrient and food group data are presented as daily averages over the three days. As most variables were positively skewed, the data are reported as medians and lower and upper quartiles ($25^{th}$ and $75^{th}$). Quantile regression was used to estimate the difference between the Control and BLISS groups for energy and nutrient intake, as well as dietary iron intake from each food group. Usual iron intake was determined,[23] and the prevalence of inadequate iron intakes was estimated using the full-probability approach.[24]

Means and standard deviations are used to describe all of the biochemical variables except plasma ferritin, CRP and AGP, which are presented as medians and lower and upper quartiles. Differences in biochemical iron status indices were estimated using regression and were adjusted for infant age at the time of blood test, infant sex, maternal education (non tertiary vs tertiary) and maternal parity (1 child vs > 1 child, including the current pregnancy). A Chi-squared test was used to compare the number of cases and controls for each of the iron status categories, and their associated odds ratios.

All analyses were conducted using statistical software Stata, version 13 (StataCorp LP, Texas, USA).

**Patient and Public Involvement**

Our interest in this area arose in part from requests from local parenting groups for advice on how to follow Baby-Led Weaning safely. In addition, a content analysis study in the same region indicated that some mothers who are following Baby-Led Weaning were concerned about whether their infant was getting enough iron.[4] Once the structure of the study had

For peer review only

been designed, the intervention resources were developed taking into account parent priorities from our pilot work.[14] Parents did not play a role in recruitment. Participants will be sent a lay summary of the results when they are published. Participant burden was not measured formally, but participants were given an opportunity to comment on the study in the final questionnaire, and another analysis is investigating the acceptability to parents of BLISS as an approach to infant feeding.

**Results**

A total of 214 mother-infant pairs were randomised, of whom eight were excluded after birth (n=5 Control, n=3 BLISS), providing a final sample size of 206 participants (**Figure 1**). Of these 206 participants, 81 Control and 88 BLISS participants provided data for this secondary analysis (**Table 1**). Baseline demographic data, and age when complementary foods were introduced, are shown in Table 1. There were no differences in the characteristics of participants who were included in this analysis (i.e. provided either intake or status data) compared with those not included (i.e. provided neither intake nor status data) with the exception of maternal age at birth, which was lower for those who did not provide data (**eTable 1**).

For peer review only

**Table 1** Characteristics of participants who provided intake data at 7 and/or 12 months of age or biochemical data at 12 months of age

| | Control (n=81) | BLISS (n=88) |
|---|---|---|
| **Maternal and household variables** | | |
| Maternal age at birth (years), mean (SD) | 32.2 (5.8) | 31.7 (4.8) |
| Maternal parity | | |
| First child | 32 (40) | 37 (42) |
| Two children | 27 (33) | 37 (42) |
| Three or more children | 22 (27) | 14 (16) |
| Maternal ethnicity | | |
| NZ European | 70 (87) | 71 (80) |
| Māori | 6 (7) | 8 (9) |
| Other | 5 (6) | 9 (10) |
| Maternal education | | |
| School only | 23 (28) | 26 (30) |
| Post-secondary | 13 (16) | 20 (22) |
| University | 45 (56) | 42 (48) |
| Household deprivation[a] | | |
| 1-3 (Low) | 24 (30) | 25 (28) |
| 4-7 | 37 (45) | 46 (53) |
| 8-10 (High) | 20 (25) | 17 (19) |
| **Infant variables** | | |
| Sex | | |
| Female | 37 (46) | 50 (57) |

For peer review only

| | | |
|---|---|---|
| Male | 44 (54) | 38 (43) |
| Infant birth weight (g), mean (SD) | 3510 (453) | 3496 (448) |
| Infant gestational age at birth (weeks), mean (SD) | 39.5 (1.2) | 39.7 (1.0) |
| **Complementary feeding variables** | | |
| Age complementary foods were introduced (weeks), mean (SD) | 22.6 (3.1) | 24.6 (3.2)[b] |
| Complementary foods delayed to 6 months of age | 15 (18) | 58 (66)[b] |

Abbreviation: NZ European; New Zealand European

Data presented as n (%), unless otherwise stated

[a]Household deprivation categorised using the NZDep2013 scale in which decile 1 indicates the lowest level of deprivation and 10 indicates the highest[25]

[b]$p<0.001$

For peer review only

Adherence to the baby-led approach was high in the BLISS group with significantly more infants feeding themselves most or all of their food in the past week at 7 (74% vs 19% Control; $p<0.001$) and 12 (77% vs 48% Control; $p<0.001$) months of age.

The differences in iron intake between the BLISS group and the Control group at 7 and 12 months were 0.6 mg/day (95% C: -1.0, 2.3) at 7 months and -0.1 mg/day (-1.6, 1.4) at 12 months (**Table 2**). In both cases the differences were small and the confidence intervals exclude clinically interesting differences. The same applies to intakes of the iron absorption modifiers that were measured, except for a significantly lower intake of Vitamin C in BLISS (49.2 mg/day) compared with Control infants (59.2 mg/day) at 7 months (adjusted difference -9.7 mg/day; 95% CI: -18.4 to -0.9). Four participants (n=2 BLISS, n=2 Control) were using iron supplements at the time of the 12-month WDR but these have not been included as the supplements were started after the blood sample was collected.

For peer review only

**Table 2** Intake of iron and key absorption modifiers at 7 and 12 months of age from complementary foods and infant milks[a]

| | Control | BLISS | Difference (95% CI)[b] | *p* Value |
|---|---|---|---|---|
| **7 months of age** | n=77 | n=85 | | |
| Energy (kJ/day), mean (SD) | 2862 (548) | 2996 (613) | 145 (-31.2, 321) | 0.11 |
| Energy from complementary foods only (kJ/day)[c], mean (SD) | 672 (506) | 799 (595) | 144 (-26.2, 314) | 0.10 |
| Dietary iron (mg/day) | 2.7 (1.3, 6.9) | 3.0 (1.5, 7.3) | 0.6 (-1.0, 2.3) | 0.46 |
| Dietary iron from complementary foods only (mg/day)[d] | 1.0 (0.5, 2.2) | 1.2 (0.7, 2.0) | 0.2 (-0.2, 0.6) | 0.34 |
| Haem iron (mg/day) | 0.0 (0.0, 0.1) | 0.0 (0.0, 0.1) | 0.0 (-0.0, 0.1) | 0.10 |
| Non-haem iron (mg/day) | 2.6 (1.3, 6.9) | 2.9 (1.4, 7.3) | 0.4 (-1.3, 2.0) | 0.67 |
| Meat, fish, poultry (g/day) | 2.8 (0.0, 11.1) | 4.3 (1.4, 8.8) | 1.3 (-1.9, 4.4) | 0.42 |
| Phytate (mg/day) | 36 (16.3, 75.2) | 45 (23.0, 77.6) | 4.2 (-15.0, 23.4) | 0.67 |
| Phytate:iron molar ratio[e] | 1.0 (0.4, 2.3) | 1.3 (0.6, 2.7) | 0.4 (-0.2, 1.0) | 0.18 |
| Vitamin C (mg/day) | 59.2 (41.7, 75.6) | 49.2 (38.3, 67.9) | -9.7 (-18.4, -0.9) | **0.032** |
| **12 months of age** | n=68 | n=75 | | |
| Energy (kJ/day), mean (SD) | 3573 (776) | 3623 (1048) | 109 (-191, 409) | 0.48 |
| Energy from complementary foods only (kJ/day)[c], mean (SD) | 2400 (848) | 2527 (1183) | 195 (-142, 533) | 0.25 |
| Dietary iron (mg/day) | 5.3 (3.1, 8.4) | 4.7 (3.1, 7.3) | -0.1 (-1.6, 1.4) | 0.87 |
| Dietary iron from complementary foods only (mg/day)[d] | 3.2 (2.3, 4.6) | 3.2 (2.5, 4.1) | -0.0 (-0.6, 0.6) | 0.94 |
| Haem iron (mg/day) | 0.2 (0.1, 0.3) | 0.2 (0.1, 0.3) | 0.0 (-0.0, 0.1) | 0.57 |
| Non-haem iron (mg/day) | 5.0 (2.9, 8.1) | 4.5 (2.9, 7.0) | -0.1 (-1.7, 1.4) | 0.85 |

For peer review only

| | | | | |
|---|---|---|---|---|
| Meat, fish, poultry (g/day) | 19.3 (7.9, 33.6) | 19.3 (11.2, 31.1) | -1.4 (-9.0, 6.2) | 0.72 |
| Phytate (mg/day) | 187 (118, 310) | 229 (152, 274) | 37 (-20.4, 94.8) | 0.20 |
| Phytate:iron molar ratio[e] | 3.8 (2.3, 6.2) | 4.3 (2.8, 6.5) | 0.6 (-0.7, 1.9) | 0.35 |
| Vitamin C (mg/day) | 48.1 (39.4, 69.5) | 50.4 (36.6, 61.4) | 0.4 (-9.4, 10.3) | 0.93 |

Data presented as median ($25^{th}$, $75^{th}$ percentile), unless otherwise stated

[a]Intake reported during the three-day weighed diet records collected at 7 and 12 months of age

[b]Difference adjusted for infant age (in days) and sex, and maternal education and parity

[c]Excludes energy from breast milk and infant formula

[d]Excludes iron from breast milk and infant formula

[e]Calculated as [phytate (mg) / 660] / [iron (mg) / 55.9]

For peer review only

There was no difference in the number of infants who were fed breast milk, formula or both, between groups at either 7 or 12 months (**eTable 2**).There were no significant differences in estimated breast milk or infant formula intake between groups at 7 (breast milk difference 0.0 g/day; 95% CI: -5.1 to 5.1; *p*=1.00; infant formula difference 216 g/day; -97.2 to 530; *p*=0.17) or 12 (breast milk difference 0.0 g/day; 95% CI: -0.1 to 0.1; *p*=0.94; infant formula difference -85 g/day; -277 to 107; *p*=0.38) months of age, and therefore no differences between groups in the contribution of infant milks to iron intake (all *p*>0.17).

BLISS infants obtained significantly more iron from 'breads and cereals', 'red meat', 'dairy', and 'legumes, nuts, seeds and eggs' than Control infants at 7 months of age (**Table 3**). For all these food groups, except 'breads and cereals', this reflected the greater proportion of BLISS infants consuming these foods (**eTable 3**). However, the differences in iron contribution were small (e.g., adjusted difference 0.1 mg iron/day from red meat; 95% CI: 0.01 to 0.1) in comparison to the Average Requirement of 5.0 mg/day[26] and therefore not likely to be clinically significant. None of the differences apparent at 7 months remained at 12 months, and although BLISS infants did receive significantly less iron from 'vegetables' than Control infants at 12 months, the actual difference was very small (-0.1 mg iron/day; 95% CI: -0.2 to -0.0) (Table 3).

For peer review only

**Table 3** Iron from complementary foods at 7 and 12 months of age (consumers and non-consumers)[a,b]

| | Control | | BLISS | | Difference (95% CI)[d] | *p* Value |
|---|---|---|---|---|---|---|
| | mg/day | %[c] | mg/day | %[c] | | |
| **7 months of age** | n=77 | | n=85 | | | |
| Vegetables | 0.16 (0.0, 0.4) | 17 (9, 25) | 0.10 (0.0, 0.2) | 8.4 (6, 17) | -0.1 (-0.1, 0.0) | 0.07 |
| Fruit and fruit juice | 0.13 (0.0, 0.2) | 11 (5, 24) | 0.09 (0.0, 0.2) | 7.2 (3, 12) | -0.0 (-0.1, 0.0) | 0.19 |
| Iron-fortified infant cereal | 0.08 (0.0, 0.7) | 7.9 (0, 54) | 0.19 (0.0, 0.5) | 19 (0, 43) | 0.1 (-0.1, 0.3) | 0.25 |
| Breads and cereals[e] | 0.09 (0.0, 0.3) | 7.2 (2, 26) | 0.26 (0.1, 0.4) | 23 (10, 35) | 0.2 (0.1, 0.2) | **<0.001** |
| Red meat[f] | 0.01 (0.0, 0.2) | 1.9 (0, 14) | 0.06 (0.0, 0.2) | 7.2 (1, 16) | 0.1 (0.0, 0.1) | **0.010** |
| Miscellaneous[g] | 0.01 (0.0, 0.1) | 1.1 (0, 6) | 0.01 (0.0, 0.1) | 1.3 (0, 6) | 0.0 (-0.0, 0.0) | 0.75 |
| Dairy | 0.00[i] (0.0, 0.0) | 0.1 (0, 0.4) | 0.00 (0.0, 0.0) | 0.5 (0, 2) | 0.0 (0.0, 0.0) | **0.010** |
| Legumes, nuts, seeds and eggs | 0.00 (0.0, 0.0) | 0.0 (0, 2) | 0.04 (0.0, 0.1) | 4.5 (1, 11) | 0.0 (0.0, 0.1) | **0.001** |
| Other meat[h] | 0.00 (0.0, 0.0) | 0.0 (0, 3) | 0.00 (0.0, 0.0) | 0.4 (0, 4) | 0.0 (-0.0, 0.0) | 0.57 |
| **12 months of age** | n=68 | | n=75 | | | |
| Breads and cereals[e] | 0.84 (0.5, 1.6) | 32 (16, 48) | 1.10 (0.6, 1.8) | 38 (27, 50) | 0.2 (-0.2, 0.5) | 0.26 |
| Vegetables | 0.38 (0.2, 0.5) | 11 (6, 16) | 0.29 (0.1, 0.5) | 8.9 (4, 14) | -0.1 (-0.2, -0.0) | **0.027** |
| Miscellaneous[g] | 0.32 (0.1, 0.6) | 9.8 (4, 18) | 0.18 (0.1, 0.5) | 5.7 (2, 17) | -0.1 (-0.3, 0.0) | 0.05 |
| Fruit and fruit juice | 0.27 (0.2, 0.5) | 8.3 (5, 13) | 0.32 (0.2, 0.5) | 10 (5, 14) | 0.0 (-0.1, 0.1) | 0.33 |
| Other meat[h] | 0.17 (0.1, 0.3) | 5.5 (2, 9) | 0.17 (0.1, 0.3) | 5.1 (1, 4) | -0.0 (-0.1, 0.1) | 0.94 |
| Legumes, nuts, seeds and eggs | 0.10 (0.0, 0.3) | 2.8 (0, 10) | 0.16 (0.0, 0.4) | 4.6 (1, 10) | 0.0 (-0.0, 0.1) | 0.28 |
| Red meat[f] | 0.09 (0.0, 0.3) | 2.5 (0, 11) | 0.15 (0.0, 0.4) | 3.8 (0, 12) | 0.1 (-0.1, 0.2) | 0.40 |
| Dairy | 0.06 (0.0, 0.1) | 1.5 (1, 4) | 0.05 (0.0, 0.1) | 1.7 (0, 4) | -0.0 (-0.0, 0.0) | 0.81 |
| Iron-fortified infant cereal | 0.00 (0.0, 0.0) | 0.0 (0, 0) | 0.00 (0.0, 0.1) | 0.0 (0, 5) | - | - |

**Bold** indicates a statistically significant difference at $p<0.05$

For peer review only

Data presented as median (25th, 75th percentile)

[a]Intake reported during the three-day weighed diet records collected at 7 and 12 months of age

[b]Ordered from highest to lowest contributor of iron to the intakes of the Control group

[c]Data expressed as median percentages (NB: *mean* percentages added to 100% of total iron intakes from complementary foods)

[d]Difference in median iron (mg/day) intake between groups: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control, adjusted for infant age (in days) and sex, and maternal education and parity

[e]Breads and cereals other than iron-fortified infant cereals

[f]Red meat defined as: beef, lamb, mutton, venison

[g]Miscellaneous defined as: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.

[h]Other meat defined as: fish, poultry, pork, processed meats

[i]Where the median intake is 0.00 this has occurred because more than half of the infants did not consume this food. Some infants did consume these foods, however, so it was possible for differences in intake to be significant. Similarly, the difference is reported as 0.00 if it is smaller than 0.05 and therefore rounds down to 0.00

For peer review only

BLISS specifically encouraged consumption of 'high-iron' foods such as red meat and iron-fortified infant cereal from the start of complementary feeding. BLISS infants were introduced to 'red meat' at the same age as Control infants (28.1 weeks, 27.9 weeks, $p$=0.74). Although significantly more BLISS than Control infants consumed 'red meat' at 7 months of age (76%, 55%; eTable 3), intakes were similarly low for consumers in both groups (BLISS 3.2 g/day, Control 3.8 g/day; **eTable 4**). BLISS infants began consuming 'iron-fortified infant cereal' approximately two weeks later than Control infants (25.4 weeks, 23.7 weeks, $p$=0.008). Interestingly, more BLISS infants were consuming 'iron-fortified infant cereal' by 7 months of age (73%, 51% Control) (eTable 3), but the median amounts consumed were very small (BLISS 1.7 g/day, Control 4.0 g/day) (eTable 4). At 12 months there were no significant differences in the number of consumers of 'iron-fortified infant cereal' or 'red meat', or in the amount consumed (**eTables 5 and 6**).

The prevalence of inadequate iron intakes was high at 74% for both groups at 7 months of age, but considerably lower by 12 months (23% Control, 26% BLISS).

The difference between the BLISS and Control groups for plasma ferritin was -2.6 µg/L (-10.9, 5.8), and not statistically significant, although the lower (and upper) confidence limits do not rule out clinically meaningful effects. Differences between the groups for the other biochemical indicators of iron status were small and not statistically significant (all $p$>0.55) (**Table 4**). Few participants had signs of inflammation/infection (n=8 Control, n=11 BLISS). The majority of infants in both groups were iron sufficient (83% Control, 83% BLISS), although 5% Control and 7% BLISS presented with iron deficiency anaemia (Table 4). Similar numbers had anaemia other than iron deficiency anaemia (13% BLISS, 10% Control; $p$=0.78).

For peer review only

Thirty-four participants had at least one biochemical value (not necessarily iron-related) outside the expected reference range for their age and were advised to contact their GP for follow up (n=19 Control, n=15 BLISS).

For peer review only

**Table 4** Iron status indicators and categories at 12 months of age

| | Control (n=59) | BLISS (n=60) | Difference (95% CI)[a] | *p* Value |
|---|---|---|---|---|
| Haemoglobin (g/L), mean (SD) | 117 (8.4) | 116 (8.9) | -0.8 (-4.0, 2.3) | 0.59 |
| Plasma ferritin (µg/L)[b] | 28.9 (18.5, 47.4) | 27.0 (19.5, 42.1) | -2.6 (-10.9, 5.8) | 0.55 |
| Soluble transferrin receptor (mg/L), mean (SD) | 7.6 (2.0) | 7.4 (2.7) | -0.2 (-1.0, 0.7) | 0.70 |
| Body iron (mg/kg)[c], mean (SD) | 3.3 (3.1) | 3.3 (2.9) | 0.04 (-1.1, 1.2) | 0.95 |
| C-reactive protein (mg/L) | 0.1 (0.0, 0.5) | 0.2 (0.1, 0.5) | -0.02 (-0.2, 0.2) | 0.86 |
| $\alpha_1$-acid glycoprotein (g/L) | 0.6 (0.4, 0.8) | 0.6 (0.5, 0.95) | 0.04 (-0.1, 0.2) | 0.56 |
| **Iron status categories, n (%)** | | | **OR (95% CI)[d]** | ***p* Value** |
| Iron sufficient[e] | 49 (83) | 50 (83) | 1.0 | - |
| Iron depleted[f] | 3 (5) | 2 (3) | 1.5 (0.2, 9.6) | 0.65 |
| Early functional iron deficiency[g] | 4 (7) | 4 (7) | 1.0 (0.2, 4.3) | 0.98 |
| Iron deficiency anaemia[h] | 3 (5) | 4 (7) | 0.8 (0.2, 3.6) | 0.74 |

Data presented as median (25th, 75th percentile), unless otherwise stated

[a]Difference adjusted for infant age (in days) and sex, and maternal education and parity: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control

[b]Ferritin adjusted for inflammation using multipliers proposed by *Thurnham et al*.[21]

[c]Body iron calculation (mg/kg) = -[log10(sTfR x 1000/ferritin) -2.8229]/0.1207 from *Cogswell et al.*[22]

[d]Odds ratio of Control relative to BLISS

[e]Defined as body iron ≥0 mg/kg, haemoglobin ≥110 g/L and plasma ferritin ≥15 µg/L

[f]Defined as plasma ferritin <15 µg/L, in the absence of early functional iron deficiency and iron deficiency anaemia

[g]Defined as body iron <0 mg/kg and haemoglobin ≥110 g/L

[h]Defined as body iron <0 mg/kg and haemoglobin <110 g/L

For peer review only

**Discussion**

We observed no significant differences in iron intake or status between infants following a baby-led approach to complementary feeding that had been modified to address concerns regarding iron intake, and infants following traditional spoon-feeding. However, iron intakes were low in both groups at 7 months (74% of infants at risk of inadequate intakes) and 17% had suboptimal iron status at 12 months.

Although many parents are choosing to follow BLW with their infant,[1-3] we know almost nothing about what these infants are eating, and how this might impact their health. Only one small observational study has evaluated intake in infants following unmodified BLW compared with age- and sex-matched infants following traditional spoon-feeding.[6] In that study, despite similar energy intakes, BLW infants had significantly lower intakes of iron than spoon-fed infants (1.6 mg/day vs 3.6 mg/day, $p<0.001$). By contrast, we found no difference in iron intakes in our study groups, and BLISS infants were consuming a median of 3.0 mg per day of iron, suggesting that encouraging the intake of 'high-iron' foods as part of a baby-led approach to complementary foods was effective in improving iron intakes.

Our BLISS intervention recommended that 'high-iron' foods, particularly red meat and iron-fortified infant cereal, should be offered at every meal, from the start of the complementary feeding period. Red meat is high in bioavailable haem iron,[27] and a higher intake has been associated with higher serum ferritin concentrations in toddlers,[28] and higher haemoglobin concentrations in very young children.[29] Similarly, iron-fortified infant cereal is high in iron and consumption has been shown to prevent iron deficiency anaemia.[30] In the current study, significantly more BLISS than Control infants were consuming red meat at 7 months. This was in contrast to an observational study suggesting that infants following unmodified

For peer review only

BLW are no more likely to consume red meat than spoon-fed infants.[6] However, actual intakes were small in both groups, as they were for iron-fortified infant cereal. Other studies have also demonstrated relatively low intakes of both red meat[31] and iron fortified foods[32] in infants and toddlers. Therefore, further research is required to determine whether a more intensive intervention can feasibly increase the amount of these important iron sources consumed by both spoon-fed and baby-led infants.

Concern has been expressed regarding dietary exposure to inorganic arsenic through infant rice cereals and the potential health risks associated with high intakes in very young children.[33] Intakes of 3.0 µg/kg body weight per day have been estimated to increase the incidence of lung cancer by 0.5%,[34] but the European Food Safety Authority (EFSA) have estimated that a 6 month old infant would have to consume 90 g of rice based cereal per day in order to be exposed to a level of inorganic arsenic of approximately half that level (1.63 µg/kg body weight).[33] Given the maximum average intake in the current study was only 7.2 g per day of infant rice cereal, and the maximum observed intake was 75 g per day, it seems very unlikely that high intakes of inorganic arsenic are an issue in this population, even when consumption of iron fortified rice cereal is encouraged.

There was a high proportion (74% of both groups) of infants at risk of inadequate iron intakes at 7 months of age. Unfortunately, we do not have a measure of iron status at 7 months to determine whether this high prevalence of inadequate intake is reflected in poor iron status. However, at 12 months of age the risk of inadequate intakes had decreased (23% of Controls, 26% of BLISS). It is possible that this high prevalence at 7 months of age may be due to the cut offs available for determining the risk of inadequate iron intakes - currently, there is no specific cut off for infants less than 8 months of age that has the Institute of Medicine

For peer review only

probabilities of inadequacy that are needed in order to calculate the prevalence of inadequacy.[35]

The BLISS study focused on iron deficiency anaemia, but 10% of Control infants and 13% of BLISS infants were diagnosed as having anaemia that was not concurrent with iron deficiency. Non-iron-deficient anaemia can be caused by a wide range of conditions, including infection (e.g., with malaria, HIV, or hookworm), folate or Vitamin B12 deficiency, or genetic disorders such as thalassemia and sickle cell anaemia.[36] We took care to minimise rates of infection in our study design, and malaria, HIV and hookworm are extremely rare in this age group in New Zealand. Similarly, no participant had a mean cell >86 fL which would be indicative of the megaloblastic anaemia of folate or Vitamin B12 deficiency.[37] We cannot rule out haemoglobinopathies as a cause of anaemia for some of the infants, but these would be fairly rare in this population. An alternative explanation for the high proportion of other anaemia could be the cut off used for defining anaemia (<110 g/L).[36,37] This value has been extrapolated from older age groups,[38] and there has been some discussion as to whether a lower cut off may be more appropriate in this age group.[39]

The current study suggests that when parents following a baby-led approach to complementary feeding are given advice to offer infants 'high-iron' foods with every meal, their iron status is similar to Control infants. This finding is important given health professionals' concerns that baby-led approaches to complementary feeding may increase the risk of iron deficiency,[3,4] and the observation that infants following unmodified BLW have significantly lower iron intakes.[6] Although we did not reach our planned sample size, it is important to note the most extreme difference in plasma ferritin concentration consistent with the data was -10.9 μg/L (i.e. the lower confidence limit for the difference). This suggests that,

For peer review only

in response to a BLISS intervention, the Control group's median plasma ferritin concentration might, at most, fall to 18.0 μg/L – a value above the cutoffs usually associated with deficiency (i.e. 12 or 15 μg/L). The data are also consistent with plasma ferritin rising to 34.7 μg/L (applying the upper confidence limit). The confidence limits for the differences in dietary iron intake at 7 and 12 months of age suggest that any differences may be too small to be of clinical interest with plausible ranges of -1 to 2.3 at 7 months and -1.6 to 1.4 at 12 months.

Our study has a number of strengths including being the first randomised controlled trial to investigate the impact of a baby-led approach to complementary feeding on iron intake and status. We collected robust dietary data using three non-consecutive days of weighed diet records. As infants often do not eat all of the food offered to them we asked parents to weigh the food before and after eating (including food that was no longer on the surface on which it was originally offered) to ensure we had as accurate a representation of actual consumption as was possible in a free-living population. The study had limited power to detect differences of 5.0 μg/L in geometric mean plasma ferritin concentrations because blood samples were obtained from 119 participants rather than the planned 168. However, the confidence intervals enable the reader to see the range of plausible differences in plasma ferritin between the groups. Also, estimated breast milk volumes were used. This approach is commonly used when other methods are not feasible[32,40-44] but does mean that we do not have specific intake values for individuals. In particular, although the estimated breast milk volumes were determined in infants who were consuming complementary foods,[18] we cannot rule out the possibility that BLISS had different effects on the amount of breast milk consumed. However, there was no evidence in the current study that BLISS impacted on the amount of infant formula consumed at 7 and 12 months of age. Finally, it was not considered ethical to randomise participants to follow an unmodified version of BLW because of concerns about its

For peer review only

safety.[3,4] Therefore, the results should not be used to make conclusions about the iron status of infants following unmodified BLW.

**Conclusions**

There was no evidence of a difference in iron intakes and status between spoon-fed infants and infants following this modified version of BLW in which parents were given advice to offer 'high-iron' foods with each meal. This suggests that a baby-led approach can be used without impacting negatively on iron status. However, it is important to note that this study assessed a modified version of BLW so no conclusions can be made about the risk of iron deficiency in infants following unmodified BLW.

**Acknowledgments**

We would like to acknowledge all the families who participated in the BLISS study, as well as the research staff involved from the Departments of Human Nutrition and Medicine at the University of Otago.

For peer review only

## Figure legend

**Figure 1.** Flow of participants through the study

## Table legend

**Table 1.** Characteristics of participants who provided intake data at 7 and/or 12 months of age or biochemical data at 12 months of age

**Table 2.** Intake of iron and key absorption modifiers at 7 and 12 months of age from complementary foods and infant milks

**Table 3.** Iron from complementary foods at 7 and 12 months of age (consumers and non-consumers)

**Table 4.** Iron status indicators and categories at 12 months of age

For peer review only

## References

1 Cameron SL, Taylor RW, Heath A-LM. Parent-led or baby-led? Associations between complementary feeding practices and health-related behaviours in a survey of New Zealand families. *BMJ Open* 2013;3:1–9.

2 Brown, Lee. A descriptive study investigating the use and nature of baby-led weaning in a UK sample of mothers. *Maternal Child Nutr* 2011;7:34–47.

3 D'Andrea E, Jenkins K, Mathews M. Baby-led Weaning: A Preliminary Investigation. *Can J Diet Pract Res* 2016;77:1–6.

4 Cameron SL, Heath A-LM, Taylor RW. Healthcare professionals' and mothers' knowledge of, attitudes to and experiences with, Baby-Led Weaning: a content analysis study. *BMJ Open* 2012;2:1–9.

5 Rapley G, Murkett T. *Baby-led Weaning: Helping your Baby to Love Good Food*. London: Vermillon 2008.

6 Morison BJ, Taylor RW, Haszard JJ, *et al.* How different are baby-led weaning and conventional complementary feeding? A cross-sectional study of infants aged 6–8 months. *BMJ Open* 2016;6:1–11.

7 Domellöf M, Braegger C, Campoy C, *et al.* Iron requirements of infants and toddlers. *J Pediatr Gastroenterol Nutr* 2014;58:119–29.

8 Lozoff B, Beard J, Connor J, *et al.* Long-Lasting Neural and Behavioral Effects of Iron Deficiency in Infancy. *Nut Rev* 2006;64:34–43.

9 Congdon EL, Westerlund A, Algarin CR, *et al.* Iron Deficiency in Infancy is Associated with Altered Neural Correlates of Recognition Memory at 10 Years. *J Pediatr* 2012;160:1027–33.

10 Taylor RW, Williams SM, Fangupo LJ, *et al.* Effect of a Baby-Led Approach to Complementary Feeding on Infant Growth and Overweight. *JAMA Pediatr* 2017;171:838-846.

11 Fangupo LJ, Heath A-LM, Williams SM, *et al.* A Baby-Led Approach to Eating Solids and Risk of Choking. *Pediatrics* 2016;138:1–10.

12 Daniels L, Heath A-LM, Williams SM, *et al.* Baby-Led Introduction to SolidS (BLISS) study: a randomised controlled trial of a baby-led approach to complementary feeding. *BMC Pediatr* 2015;15:1–15.

13 Ministry of Health New Zealand. Well Child/Tamariki Ora services. Wellington: 2014 (accessed 30 July 2017). http://www.health.govt.nz/our-work/life-stages/child-health/well-child-tamariki-ora-services

14 Cameron SL, Taylor RW, Heath A-LM. Development and pilot testing of Baby-Led Introduction to SolidS - a version of Baby-Led Weaning modified to address concerns about iron deficiency, growth faltering and choking. *BMC Pediatr* 2015;15:1–11.

For peer review only

15 Ministry of Health New Zealand. New Zealand food composition database (FOODfiles). 2010 (accessed 4 July 2014). www.foodcomposition.co.nz/foodfiles.

16 Ministry of Health New Zealand, University of Otago New Zealand. Methodology report for the 2008/09 New Zealand adult nutrition survey. Wellington: Ministry of Health, 2011 (accessed 20 April 2017). http://www.health.govt.nz/publication/methodology-report-2008-09-nz-adult-nutrition-survey9-new-zealand-adult-nutrition-survey/oclc/756914555

17 Clousten A. *The role of commercial processed baby foods in the diets of New Zealand toddlers*. Thesis, Master of Dietetics. University of Otago, New Zealand. 2014. http://hdl.handle.net/10523/5492.

18 Dewey KG, Heinig MJ, Nommsen LA, *et al.* Adequacy of energy intake among breast-fed infants in the DARLING study: relationships to growth velocity, morbidity, and activity levels. *J Pediatr* 1991;119:538–47.

19 Barris A. *Meat and haem iron intakes of New Zealand toddlers aged 12-24 months*. Thesis, Master of Dietetics. University of Otago, New Zealand. 2012. http://hdl.handle.net/10523/3839.

20 Hartley N. *Phytate and zinc intakes of toddlers from New Zealand*. Thesis, Master of Dietetics. University of Otago, New Zealand. 2013. http://hdl.handle.net/10523/4645.

21 Thurnham DI, McCabe LD, Haldar S, *et al.* Adjusting plasma ferritin concentrations to remove the effects of subclinical inflammation in the assessment of iron deficiency: a meta-analysis. *Am J Clin Nutr* 2010;92:546–55.

22 Cogswell ME, Looker AC, Pfeiffer CM, *et al.* Assessment of iron deficiency in US preschool children and nonpregnant females of childbearing age: National health and nutrition examination survey 2003-2006. *Am J Clin Nutr* 2009;89:1334–42.

23 Harttig U, Haubrock J, Knüppel S, *et al.* The MSM program: web-based statistics package for estimating usual dietary intake using the Multiple Source Method. *Eur J Clin Nutr* 2011;65:S87–S91.

24 Gibson RS, Ferguson EL. An interactive 24-hour recall for assessing the adequacy of iron and zinc intakes in developing countries. *HarvestPlus Technical Monograph* 2008:1–160.

25 Atkinson J, Salmond C, Crampton P. *NZDep2013 Index of Deprivation User's Manual*. Department of Public Health, University of Otago, Wellington and Division of Health Sciences, University of Otago, New Zealand 2014.

26 European Food Safety Authority (EFSA) Panel on Dietetic Products Nutrition and Allergies. Scientific Opinion on Dietary Reference Values for Iron. 2015:1–115.

For peer review only

27 Lombardi-Boccia G, Dominguez BM, Aguzzi A. Total heme and non-heme iron in raw and cooked meats. *Food Chem Toxicol* 2002;67:1–4.

28 Szymlek-Gay EA, Ferguson EL, Heath A-LM, *et al.* Food-based strategies improve iron status in toddlers: a randomized controlled trial. *Am J Clin Nutr* 2009;90:1541–51.

29 Olaya GA, Lawson M, Fewtrell MS. Efficacy and safety of new complementary feeding guidelines with an emphasis on red meat consumption: a randomized trial in Bogota, Colombia. *Am J Clin Nutr* 2013;98:983–93.

30 Walter T, Dallman PR, Pizarro F, *et al.* Effectiveness of iron-fortified infant cereal in prevention of iron-deficiency anemia. *Pediatrics* 1993;91:976–82.

31 Fox MK, Reidy K, Novak T, *et al.* Sources of Energy and Nutrients in the Diets of Infants and Toddlers. *J Am Diet Assoc* 2006;106:S28–S42.

32 Wall CR, Brunt DR, Grant CC. Ethnic variance in iron status: is it related to dietary intake? *PHN* 2008;12:1413–21.

33 European Food Safety Authority (EFSA) Panel on Contaminants in the Food Chain (CONTAM). Scientific Opinion on Arsenic in Food. *EFSA Journal* 2009;7:1351–199.

34 World Health Organization. Joint FAO/WHO Expert Committee On Food Additives: Summary and Conclusions. 2010:1–16.

35 Institute of Medicine, Food and Nutrition Board. *Dietary reference intakes: vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc*. Washington, DC: National Academy Press 2001.

36 World Health Organization. *Iron deficiency anaemia: assessment, prevention and control: a guide for programme managers*. Geneva: World Health Organization 2001.

37 Southern Community Laboratories Ltd. Southern Community Laboratories Paediatric Reference Ranges. Southern Community Laboratories 2014.

38 Gibson RS. *Principles of Nutritional Assessment: Chapter 17 Assessment of iron status*. 2nd ed. New York: Oxford University Press 2005.

39 Domellöf M, Dewey KG, Lönnerdal B, *et al.* The diagnostic criteria for iron deficiency in infants should be reevaluated. *J Nutr* 2002;132:3680–6.

40 Skinner JD, Carruth BR, Houck KS, *et al.* Longitudinal Study of Nutrient and Food Intakes of Infants Aged 2 to 24 Months. *J Am Diet Assoc* 1997;97:496–504.

41 Devaney B, Ziegler P, Pac S, *et al.* Nutrient intakes of infants and toddlers. *J Am Diet Assoc* 2004;104:S14–S21.

42 Ponza M, Devaney B, Ziegler P, *et al.* Nutrient intakes and food choices of

For peer review only

infants and toddlers participating in WIC. *J Am Diet Assoc* 2004;104:S71–9.

43 Briefel RR, Kalb LM, Condon E, *et al.* The Feeding Infants and Toddlers Study 2008: Study Design and Methods. *J Am Diet Assoc* 2010;110:S16–S26.

44 Sharma S, Kolahdooz F, Butler L, *et al.* Assessing dietary intake among infants and toddlers 0–24 months of age in Baltimore, Maryland, USA. *Nutr J* 2013;12:1–7.

For peer review only

**Contributorship Statement:**

A-LMH and RWT conceived and designed the research. LD contributed to the design of the iron-related components of the research, collected data, and prepared the first full and subsequent drafts of this manuscript. SMW and JJH advised on study design and performed statistical analyses. RSG, EAF, BJW and BJT provided expert input into the design of the study and ongoing advice and support. All authors made an important intellectual contribution to this manuscript, and approved the final manuscript as submitted.

For peer review only

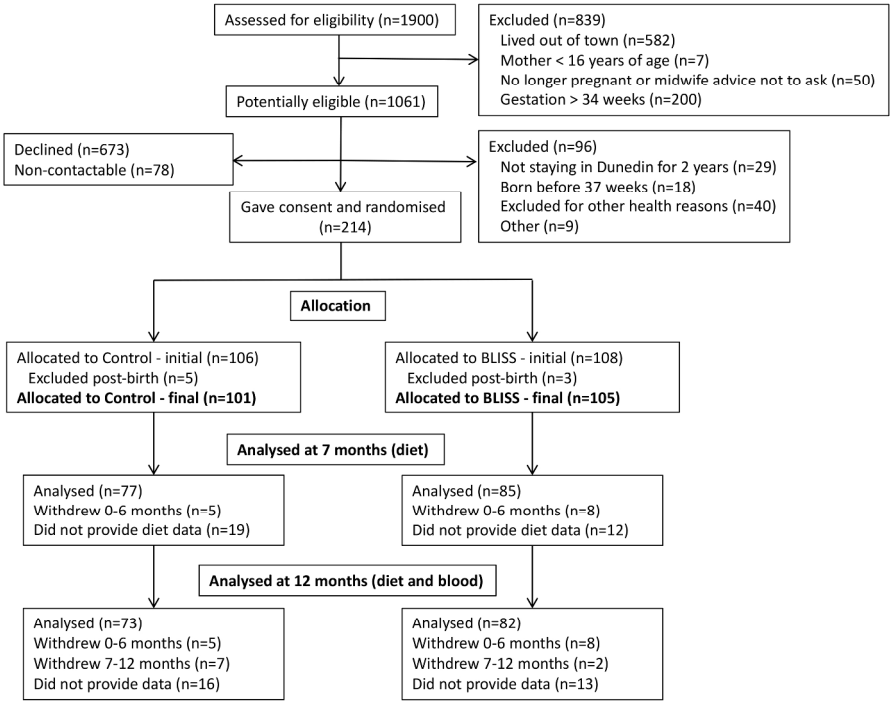



Figure 1. Flow of participants through the study

254x190mm (300 x 300 DPI)

For peer review only

## Supplemental Tables

**eTable 1** Comparison of characteristics of participants who provided either intake or status data so were included in this analysis, and whose who provided neither intake nor status data so were not included.

**eTable 2** Milk consumers at 7 and 12 months of age

**eTable 3** Number of consumers of each food group at 7 months of age

**eTable 4** Dietary sources of iron for consumers only at 7 months of age (complementary foods and infant milks)

**eTable 5** Number of consumers of each food group at 12 months of age

**eTable 6** Dietary sources of iron for consumers only at 12 months of age (complementary foods and infant milks)

For peer review only

**eTable 1** Comparison of characteristics of participants included (provided either intake or status data) and not included (provided neither intake nor status data)[a]

| | Included (*n*=169) | Not included (*n*=37) | *p* |
|---|---|---|---|
| **Maternal and household variables** | | | |
| Maternal age at birth (years), mean (SD) | 31.9 (5.3) | 28.3 (5.8) | **<0.001** |
| Maternal parity | | | 0.79 |
| First child | 69 (41) | 16 (43) | |
| Two children | 64 (38) | 11 (30) | |
| 3 or more children | 36 (21) | 10 (27) | |
| Maternal ethnicity | | | 0.45 |
| NZ European | 141 (83) | 27 (73) | |
| Māori | 14 (8.5) | 6 (16) | |
| Other | 14 (8.5) | 4 (11) | |
| Maternal education | | | 0.29 |
| School only | 49 (29) | 14 (38) | |
| Post-secondary | 33 (20) | 10 (27) | |
| University | 87 (51) | 13 (35) | |
| Household deprivation[b] | | | 0.92 |
| 1-3 (Low) | 49 (29) | 11 (30) | |
| 4-7 | 83 (49) | 19 (51) | |
| 8-10 (High) | 37 (22) | 7 (19) | |

For peer review only

| | Included (*n*=169) | Not included (*n*=37) | *p* |
|---|---|---|---|
| **Infant variables** | | | |
| Sex | | | 0.29 |
| Female | 87 (51) | 22 (61) | |
| Male | 82 (49) | 14 (39) | |
| Infant birth weight (g), mean (SD) | 3503 (449) | 3619 (545) | 0.18 |
| Infant gestational age at birth (weeks), mean (SD) | 39.6 (1.1) | 39.6 (1.0) | 0.95 |

Abbreviations: NZ European, New Zealand European

**Bold** indicates a statistically significant difference at $p<0.05$

[a]Data presented as *n* (%), unless otherwise stated

[b]Household deprivation categorised using the NZDep2013 scale in which decile 1 indicates the lowest level of deprivation and 10 indicates the highest[25]

For peer review only

**eTable 2** Milk consumers at 7 and 12 months of age[a,b]

| | Total | Control | BLISS | *p* Value |
|---|---|---|---|---|
| **7 months of age** | n=162 | n=77 | n=85 | |
| Breast milk only | 82 (51) | 38 (49) | 44 (52) | 0.95 |
| Infant formula only | 39 (24) | 19 (25) | 20 (23) | |
| Mixed (breast milk and infant formula) | 41 (25) | 20 (26) | 21 (25) | |
| **12 months of age** | n=143 | n=68 | n=75 | |
| Breast milk only | 62 (43) | 31 (46) | 31 (41) | 0.94 |
| Infant formula only | 47 (33) | 22 (32) | 25 (33) | |
| Mixed (breast milk and infant formula) | 15 (11) | 7 (10) | 8 (11) | |
| None of the above | 19 (13) | 8 (12) | 11 (15) | |
| Cow's milk[c] | | | | |
| None | 92 (64) | 47 (69) | 45 (60) | 0.51 |
| < 500mL/day | 40 (28) | 17 (25) | 23 (31) | |
| ≥ 500mL/day | 11 (8) | 4 (6) | 7 (9) | |

[a]Data presented as n (%)
[b]Based on intake reported during the three-day weighed diet records, collected at 7 and 12 months of age
[c]Cow's milk consumed as a drink

For peer review only

**eTable 3** Number of consumers of each food group at 7 months of age[a,b,c]

| | Control | BLISS | *p* Value |
|---|---|---|---|
| Breads and cereals[d] | 77 (100) | 85 (100) | - |
| Miscellaneous[e] | 77 (100) | 85 (100) | - |
| Vegetables | 75 (97) | 84 (99) | 0.50 |
| Fruit and fruit juice | 73 (95) | 81 (95) | 0.89 |
| Dairy | 66 (86) | 82 (96) | **0.015** |
| Breast milk | 58 (75) | 65 (76) | 0.87 |
| Red meat[f] | 42 (55) | 65 (76) | **0.003** |
| Iron-fortified infant cereal | 39 (51) | 62 (73) | **0.003** |
| Infant formula | 39 (51) | 41 (48) | 0.76 |
| Other meat[g] | 38 (49) | 45 (53) | 0.65 |
| Legumes, nuts, seeds and eggs | 26 (34) | 71 (84) | **<0.001** |

[a]Data presented as n (%)
[b]Intake reported during the three-day weighed diet records collected at 7 months of age
[c]Ordered by number of consumers in the Control group from highest to lowest
[d]Breads and cereals other than iron-fortified infant cereals
[e]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.
[f]Red meat defined as: beef, lamb, mutton, venison
[g]Other meat defined as: fish, poultry, pork, processed meats

For peer review only

**eTable 4** Dietary sources of iron for consumers only[a] at 7 months of age (complementary foods and infant milks)[b,c,d]

| | Control | | BLISS | | Difference (95% CI)[e] | *p* Value |
|---|---|---|---|---|---|---|
| | g/day | mg/day | g/day | mg/day | | |
| Infant formula | 309 (110, 745) | 5.5 (1.2, 8.3) | 525 (136, 804) | 6.0 (2.7, 7.5) | 0.5 (-2.0, 3.0) | 0.70 |
| Iron-fortified infant cereal | 4.0 (2, 9) | 0.72 (0.3, 1.3) | 1.7 (0.5, 5) | 0.37 (0.1, 0.9) | -0.3 (-0.7, -0.0) | **0.041** |
| Breast milk | 750 (660, 750) | 0.52 (0.46, 0.53) | 750 (660, 750) | 0.52 (0.48, 0.53) | 0.0 (-0.0, 0.0) | 0.99 |
| Vegetables | 34.8 (12, 72) | 0.16 (0.1, 0.4) | 20.5 (10, 43) | 0.10 (0.0, 0.2) | -0.06 (-0.1, 0.0) | 0.06 |
| Fruit and fruit juice | 55.6 (19, 94) | 0.14 (0.1, 0.3) | 39.5 (16, 69) | 0.10 (0.0, 0.2) | -0.0 (-0.1, 0.0) | 0.21 |
| Red meat[f] | 3.8 (1, 9) | 0.13 (0.0, 0.4) | 3.2 (1, 6) | 0.11 (0.0, 0.2) | -0.0 (-0.1, 0.1) | 0.50 |
| Breads and cereals[g] | 7.8 (2, 18) | 0.11 (0.0, 0.3) | 15.5 (8, 28) | 0.26 (0.1, 0.4) | 0.15 (0.1, 0.2) | **<0.001** |
| Legumes, nuts, seeds and eggs | 3.7 (1, 7) | 0.06 (0.01, 0.2) | 3.1 (1, 9) | 0.05 (0.0, 0.2) | -0.0 (-0.1, 0.0) | 0.41 |
| Other meat[h] | 3.6 (2, 8) | 0.04 (0.01, 0.1) | 4.7 (2, 9) | 0.04 (0.02, 0.1) | 0.0 (-0.0, 0.0) | 0.90 |
| Miscellaneous[i] | 40.0 (10, 85) | 0.01 (0.0, 0.1) | 32.8 (10, 61) | 0.02 (0.0, 0.1) | -0.0 (-0.0, 0.0) | 0.99 |
| Dairy | 10.8 (0.4, 29) | 0.0 (0.0, 0.0) | 9.4 (2, 24) | 0.0 (0.0, 0.0) | 0.0 (-0.0, 0.0) | 0.27 |

[a]Refer to eTable 3 for the number of consumers of each food group at 7 months of age
[b]Data presented as median (25$^{th}$, 75$^{th}$ percentile)
[c]Intake reported during the three-day weighed diet records collected at 7 months of age
[d]Ordered from highest to lowest food group contributing to total iron intakes in the Control group
[e]Difference in median iron (mg/day) intake between groups: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control
[f]Red meat defined as: beef, lamb, mutton, venison
[g]Breads and cereals other than iron-fortified infant cereals
[h]Other meat defined as: fish, poultry, pork and processed meats
[i]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.

For peer review only

**eTable 5** Number of consumers of each food group at 12 months of age[a,b,c]

| | Control | BLISS | *p* Value |
|---|---|---|---|
| Breads and cereals[d] | 68 (100) | 75 (100) | - |
| Miscellaneous[e] | 68 (100) | 75 (100) | - |
| Dairy | 68 (100) | 74 (99) | 0.34 |
| Vegetables | 67 (99) | 75 (100) | 0.29 |
| Fruit and fruit juice | 66 (97) | 72 (96) | 0.73 |
| Other meat[f] | 57 (84) | 67 (89) | 0.33 |
| Legumes, nuts, seeds and eggs | 55 (81) | 66 (88) | 0.24 |
| Red meat[g] | 41 (60) | 53 (71) | 0.19 |
| Breast milk | 38 (56) | 39 (52) | 0.64 |
| Infant formula | 29 (43) | 33 (44) | 0.87 |
| Iron-fortified infant cereal | 14 (21) | 21 (28) | 0.30 |

[a]Data presented as n (%)
[b]Intake reported during the three-day weighed diet records collected at 12 months of age
[c]Ordered by number of consumers in the Control group from highest to lowest
[d]Breads and cereals other than iron-fortified infant cereals
[e]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.
[f]Other meat defined as: fish, poultry, pork, processed meats
[g]Red meat defined as: beef, lamb, mutton, venison

For peer review only

**eTable 6** Dietary sources of iron for consumers only[a] at 12 months of age (complementary foods and infant milks)[b,c,d]

| | Control | | BLISS | | Difference (95% CI)[e] | *p* Value |
|---|---|---|---|---|---|---|
| | g/day | mg/day | g/day | mg/day | | |
| Infant formula | 414 (274, 569) | 4.9 (3.5, 6.4) | 329 (87, 524) | 3.8 (1.5, 5.4) | -1.1 (-2.9, 0.7) | 0.23 |
| Iron-fortified infant cereal | 7.2 (3, 15) | 1.2 (0.6, 3.5) | 3.3 (2, 5) | 0.73 (0.4, 1.2) | -0.7 (-1.8, 0.4) | 0.22 |
| Breads and cereals[f] | 57.1 (39, 74) | 0.84 (0.5, 1.6) | 60.2 (47, 82) | 1.10 (0.6, 1.8) | 0.2 (-0.2, 0.5) | 0.26 |
| Vegetables | 64.6 (45, 97) | 0.39 (0.2, 0.5) | 55.5 (26, 73) | 0.29 (0.1, 0.5) | -0.1 (-0.2, -0.0) | **0.023** |
| Miscellaneous[g] | 132 (89, 205) | 0.32 (0.1, 0.6) | 119 (67, 235) | 0.18 (0.1, 0.5) | -0.1 (-0.3, 0.0) | 0.05 |
| Breast milk | 448 (448, 448) | 0.31 (0.3, 0.31) | 448 (443, 448) | 0.31 (0.3, 0.31) | -0.0 (-0.0, 0.0) | 0.54 |
| Fruit and fruit juice | 94.4 (52, 132) | 0.27 (0.2, 0.5) | 106 (60, 165) | 0.32 (0.2, 0.5) | 0.1 (-0.0, 0.2) | 0.31 |
| Red meat[h] | 9.2 (5, 19) | 0.27 (0.1, 0.6) | 9.4 (4, 15) | 0.28 (0.1, 0.5) | 0.0 (-0.2, 0.2) | 0.89 |
| Other meal[i] | 17.7 (8, 28) | 0.21 (0.1, 0.3) | 15.7 (8, 27) | 0.19 (0.1, 0.3) | -0.0 (-0.1, 0.1) | 0.64 |
| Legumes, nuts, seeds and eggs | 7.2 (3, 25) | 0.14 (0.0, 0.4) | 11.2 (5, 23) | 0.20 (0.1, 0.4) | 0.1 (-0.0, 0.2) | 0.27 |
| Dairy | 84.4 (34, 188) | 0.06 (0.0, 0.1) | 109 (51, 188) | 0.06 (0.0, 0.1) | 0.0 (-0.0, 0.0) | 0.82 |

[a]Refer to eTable 5 for the number of consumers of each food group at 12 months of age
[b]Data presented as median (25$^{th}$, 75$^{th}$ percentile)
[c]Intake reported during the three-day weighed diet records collected at 12 months of age
[d]Ordered from highest to lowest food group contributing to total iron intakes in the Control group
[e]Difference in median iron (mg/day) intake between groups: negative values represent lower values in BLISS than in Control, positive values represent higher values in BLISS than in Control
[f]Breads and cereals other than iron-fortified infant cereals
[g]Miscellaneous includes: fats, sugar, sweet foods, herbs and spices, sauces, spreads, beverages etc.
[h]Red meat defined as: beef, lamb, mutton, venison
[i]Other meat defined as: fish, poultry, pork, processed meats

For peer review only

## Checklist of items to include when reporting a randomized trial (56-58)

| PAPER SECTION<br>And topic | Item | Description | Reported on page # |
|---|---|---|---|
| *TITLE & ABSTRACT* | 1 | How participants were allocated to interventions (*e.g.*, "random allocation", "randomized", or "randomly assigned"). | 1, 5 |
| *INTRODUCTION*<br>Background | 2 | Scientific background and explanation of rationale. | 7 |
| *METHODS*<br>Participants | 3 | Eligibility criteria for participants and the settings and locations where the data were collected. | 8 |
| Interventions | 4 | Precise details of the interventions intended for each group and how and when they were actually administered. | 8-9 |
| Objectives | 5 | Specific objectives and hypotheses. | 7 |
| Outcomes | 6 | Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors). | 7 |
| Sample size | 7 | How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules. | 12 |
| Randomization --<br>Sequence generation | 8 | Method used to generate the random allocation sequence, including details of any restriction (*e.g.*, blocking, stratification). | 8 |
| Randomization --<br>Allocation concealment | 9 | Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned. | 8 |
| Randomization --<br>Implementation | 10 | Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups. | 8 |
| Blinding (masking) | 11 | Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. When relevant, how the success of blinding was evaluated. | 10 |
| Statistical methods | 12 | Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses. | 12-13 |
| RESULTS<br><br>Participant flow | 13 | Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons. | Figure 1 |
| Recruitment | 14 | Dates defining the periods of recruitment and follow-up. | 8, Figure 1 |
| Baseline data | 15 | Baseline demographic and clinical characteristics of each group. | Table 1 |
| Numbers analyzed | 16 | Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat" . State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%). | 12, tables |
| Outcomes and estimation | 17 | For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval). | 13-15 |
| Ancillary analyses | 18 | Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory. | 13-15 |
| Adverse events | 19 | All important adverse events or side effects in each intervention group. | 12 |
| DISCUSSION<br>Interpretation | 20 | Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes. | 15-18 |
| Generalizability | 21 | Generalizability (external validity) of the trial findings. | 15-18 |
| Overall evidence | 22 | General interpretation of the results in the context of current evidence. | 15-18 |

For peer review only